Archives of Disease in Childhood 1991; 66: 584–587

Is low birth weight a risk factor for asthma during adolescence?

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Abstract

The effect of low birth weight on the incidence of asthma by 17 years of age was investigated by studying medical draft examination records of 20 312 male subjects born in Jerusalem between January 1967 and December 1971. Additional information on birth weight and other demographic factors was abstracted from the Jerusalem Perinatal Study computerised database. A stepwise multiple logistic regression was used to estimate the odds ratios for developing asthma by 17 years of age in 500 g birthweight categories from <2000 g to 4500 g. The odds ratios were adjusted for the confounding effects of ethnic origin, social class (determined by area of residence), paternal education, maternal age, and birth order. The group with low birth weights (<2500 g, n=1004) had a significantly increased risk of developing asthma by 17 years of age, with an adjusted odds ratio of 1·44 (95% confidence interval (CI) 0·79 to 2·66) for birthweight group <2000 g and 1·49 (95% CI 1·05 to 2·12) for birthweight group 2000–2499 g compared with the reference group of 3000–3499 g.

We conclude that infants with birth weights of <2500 g may have a higher risk of asthma during childhood and adolescence than infants who were heavier at birth.

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Accepted 13 December 1990

Advances in neonatal intensive care have greatly improved the survival of low birthweight (LBW) infants, but they still have a high risk of handicaps.[1 2] Currently little is known about the long term respiratory outcome of LBW infants. Chan *et al* reported a close association between low birth weight and poor airway function,[3] and troublesome cough at 7 years of age.[4]

The aim of this study was to evaluate the influence of low birth weight on the incidence of asthma during childhood and adolescence. The possible effects of social, ethnic, and environmental factors were taken into account.

Subjects and methods

The computerised records of the medical examinations of 20 312 male recruits to the Israeli army who were born in Jerusalem between 1964 and 1971 were reviewed to establish the incidence of asthma. Each subject had been asked specifically whether he had ever been diagnosed as having asthma and whether he had ever had recurrent wheezing, nocturnal coughing, or coughing or wheezing after exertion (I Auerbach, C Springer, S Godfrey, personal communication). All those with any symptoms that could have been indicative of past or present asthma were referred for a second examination by a pulmonologist. This examination included a further detailed history, physical examination, and spirometry while at rest. An exercise test was done during the latter period of our study in all subjects except those who had overt signs of obstruction on spirometry. The specific information about lung function information is not available, however, as the computerised data included only the final diagnosis.

Asthma was diagnosed only in cases with clear medical evidence of past or present bronchial disease, as opposed to episodic attacks. Birth weights recorded at the time of delivery were obtained from the computerised files of the Jerusalem Perinatal Study.[5 6] Detailed demographic data were available from the computerised records of the military draft medical examination.[7] The data for each individual were matched using a seven digit identification number. The completeness of the match was confirmed by comparing maternal identity numbers.

A stepwise multiple logistic regression analysis was done with the Logist procedure of the SAS software to adjust for the effect of the studied independent variables.[8] Asthma was used as the dependent variable. The independent variables were birth weight (in 500 g categories from <2000 g–4500 g), ethnic origin (according to paternal country of birth), area of residence (classified by municipal tax level),[6] maternal age (as a continuous variable), paternal educational attainment (years of schooling) and birth order (categorised to avoid dubious assumptions about linearity). All variables that were significant ($p<0·05$) were added to a model that contained the birth weight variable at the first step.

The results of the logistic regressions are presented as adjusted odds ratios with their 95% confidence intervals (CI). The estimates presented are based on the exclusion of cases with missing values (1·9%).

Results

The overall incidence of asthma in our study population at 17 years of age was 3·7%. Subjects whose birth weight was between 2000–2499 g had a significantly higher incidence of asthma. Other factors that were associated with a significantly increased risk of asthma included European or North American ethnic origin, being the first born, and having a well educated father (table 1). There was a significantly lower incidence of asthma among subjects who were of Asian origin, who were high in the birth order, and whose fathers were less well educated (table 1). Obesity and area of residence were not related to the incidence of asthma.

To estimate the risk of asthma associated with birth weight a multiple logistic regression analysis was used to control for the effects of confounding variables. All the variables listed in table 1 were analysed. The final model reached by the stepwise procedure included the birth weight variable and four confounding variables: birth order, paternal education, maternal age, and ethnic origin. Logistic analysis of these data confirmed that there was a highly significantly increased risk of asthma at 17 years of age for those with birth weights of less than 2500 g (table 2).

Table 1 Distribution of population characteristics and incidence of asthma at 17 years of age among 20 312 male subjects born in Jerusalem, 1967–71

Population characteristics	*Percentage of total population*	*Percentage with asthma*
Ethnic origin (paternal country of birth):		
Israel	14·9	3·8
Asia	33·3	2·7*
Africa	23·5	3·3
Europe or North America	28·3	4·8*
Paternal educational attainment (years of schooling):		
<8	37·2	2·7*
8–12	38·7	4·1*
>12	24·1	5·1
Birth order:		
1	28·2	5·0*
2	23·3	3·9
3–4	26·8	3·4
≥5	21·7	2·0*
Area of residence (municipal tax level):		
High	26·3	4·1
Medium	33·8	4·0
Low	39·9	3·0
Birth weight (g):		
<2000	1·1	5·8
2000–2499	3·6	5·3**
2500–2999	16·3	4·1
3000–3499	41·2	3·6
3500–3999	28·8	3·4
4000–4499	7·8	3·5
>4500	1·2	3·9
Body mass index (kg/m^2):		
>24·6	10·2	4·2
≤24·6	89·8	3·6
Total	100	3·7

*p<0·001; **p<0·01 (χ^2 test).

Discussion

The present study is the first to our knowledge that examines the incidence of asthma in association with birth weight in a large population for a period of 17 years. Low birth weight was associated with asthma diagnosed up to 17 years of age. Such an association has been suggested previously,[9] and the need for long term follow up was stressed.[10] Most previous studies have shown that small groups of infants who survive specific neonatal respiratory complications and treatments, including bronchopulmonary dysplasia,[11 12] hyaline membrane disease,[13–15] or artificial ventilation have reduced airway function.[16–19] In some studies, however, impairment in lung function has been observed in healthy LBW infants as well.[20] Furthermore, long term follow up studies extending to school age have shown that abnormal lung function is not unusual among LBW children.[3 4 17 18 21] The association between low birth weight and poor airway function is independent of neonatal respiratory illness, oxygen treatment, or mechanical ventilation.[3 4] Perinatal factors, including the amount of respiratory support, were found to make only a small contribution to the reduction in airway function found in children of low birth weight at the ages of 7[22] and 9[23] years.

A number of possible explanations for the link between low birth weight and asthma have been proposed. The reduced airway function has been attributed to constitutional factors, prematurity itself, or other undetermined factors.[23] The airway hyperactivity found at 7 and 12 years of age in prematurely born children without neonatal lung disease, led Bertrand *et al* to speculate that unexplained premature labour may share a common pathway with airway lability.[24] In the present study we could not take into account the family history of asthma. Chan *et al*, in a prospective study on a cohort of 7 year old children of low birth weight, found an increased prevalence of airway responsiveness to histamine that was significantly related to a history of asthma in siblings,[25] but they were unable to confirm the hypothesis that maternal smooth muscle irrita-

Table 2 Adjusted odds ratios for asthma at 17 years of age by birth weight, ethnic origin, area of residence, maternal age, paternal education, and birth order for 20 312 male subjects born in Jerusalem, 1964–71

Variable	*No of subjects*	*Adjusted odds ratios*	*95% confidence intervals*
Birth weight (g):			
<2000	223	1·44	(0·79 to 2·62)
2000–2499	781	1·49 (p<0·001)	(1·05 to 2·12)
2500–2999	3311	1·09	(0·89 to 1·35)
3000–3499*	8369	1·00	
3500–3999	5160	0·97	(0·81 to 1·17)
4000–4499	1584	1·11	(0·83 to 1·49)
>4500	244	1·30	(0·73 to 2·67)
Birth order:			
1	5727	0·72 (p<0·001)	(0·59 to 0·89)
2*	4733	1·00	
3–4	5444	0·58 (p<0·001)	(0·47 to 0·73)
≥5	4408	0·33 (p<0·001)	(0·24 to 0·45)
Paternal education (years):			
<8	7556	†	
8–12*	7861	1·00	
>12	4895	1·33 (p<0·001)	(1·13 to 1·58)
Ethnic origin:			
Israel*	3027	1·00	
Asia	6764	0·81 (p<0·05)	0·66 to 0·99)
Africa	4773	†	
Europe or North America	5748		

*Reference group; †variable not significant in the final logistic model.

bility (uterine and bronchial) has a causative role in either the premature labour or in the subsequent airway hyper-responsiveness in the prematurely born infants.

The excess risk of asthma may also be the outcome of acute lower respiratory tract infections in infancy including bronchitis, bronchiolitis and pneumonia,[26–28] which are known to be more common among LBW children.[12] Asthma has also been related to other diseases of infancy including throat or ear infections, eczema, and allergic rhinitis,[29] all reported more frequently among LBW infants.[30]

Area of residence, social class, and family size are associated with a history of upper[31] and lower[32–35] respiratory tract infections. Because the incidence LBW infants is increased among families in low socioeconomic groups,[36 37] poor environmental conditions may explain the observed link between LBW and asthma in childhood and adolescence. It is interesting to note that while Burr found that having more siblings increased the likelihood of prolonged colds, and of wheeze and nasal discharge.[38] Strachan showed a strong inverse relationship between hay fever and the number of children in the household at the age of 11.[39] The present results show a decreased risk of asthma for children of high birth order, which accords with the atopic nature of the disease. The higher incidence of asthma in smaller households may be a possible explanation for the current increase in the prevelance of asthma.[8 38 39]

Maternal smoking in pregnancy is a major determinant of birth weight,[36 40] and its intrauterine effects may be related to lower respiratory tract illness in early life.[41] Furthermore, LBW infants affected by maternal and environmental (passive) smoking antenatally are more likely to be exposed to tobacco smoke during childhood.[42] This may lead to an increased incidence of respiratory illness[43] and aggravation of asthma.[38 44 45] Data on the incidence of smoking among our sample was not available, but as adolescents born to mothers that smoke are more prone to do so themselves, they are also more likely to have been born with a lower birth weight and subsequently to have bronchial disease as a result of their smoking. Smoking by both the mothers and the subjects themselves may thus confound the association between low birth weight and asthma.

Birth weight could not be corrected for gestational age in the present sample, so it was not possible to find out if the increased risk of asthma was related to intrauterine growth retardation or immaturity. Nevertheless, low birth weight remains an important indicator of neonatal outcome.

In the present study, a large population from a geographically defined area was evaluated. The results may thus reflect the later effect of low birth weight on pulmonary function in relation to the incidence in our population. Population studies are important, as estimates of the incidence of asthma in childhood vary widely as a result of the different diagnostic labels given.[46 47] Our findings indicate that LBW infants have an increased risk of asthma in childhood and adolescence. Further research is necessary to improve our understanding of the factors that predispose low birthweight infants to asthma in later life.

We acknowledge financial assistance from the Doron Foundation.

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Ban it!

The 'ban it' lobby are at it again, I see. Their target this time is toy balloons. Children sometimes inhale them, as they inhale many other things. A paper from Alberta (Ryan *et al*, *American Journal of Diseases of Children* 1990;**144**:1221–4) documents four deaths in Canada between 1983 and 1988. In the United States there were 121 childhood deaths from balloon inhalation between 1973 and 1988. The authors comment that 'protective efforts should be directed to a ban on this type of balloon'.

Most children who choke do so on food. Of those who choke on other things 90% do so on household articles, such as nails or bolts, and the remaining 10% inhale toys or other 'children's products'. Of this 10%, 43% involves balloons. Balloons are therefore 'the leading cause of paediatric choking deaths from children's products'.

Of course, if you go on subcategorising long enough almost anything can be shown to be the leading cause of something or other. Most of the road deaths in Britain not involving British, French, German, Swedish, or Italian cars probably involve Japanese cars which should, of course, therefore be banned.

I am 200% in favour of preventing childhood accidents but consider the pleasure given to so many children (and adults) by toy balloons. It is not possible to ban everything a child might put into his mouth or choke on. By all means let's educate people, children, and adults. Children choke; be careful. Don't leave things around or let them play with things they might choke on. Be careful with balloons; be careful with marbles; be careful with boiled sweets. Be careful, be careful, please be careful. But ban balloons? Must we?

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