ORIGINAL ARTICLE

Birth anthropometric measures, body mass index and allergic diseases in a birth cohort study (BAMSE)

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Objective: We aimed to assess increased birth weight or birth length in relation to allergic diseases at 4 years of age, taking body mass index (BMI) at age 4 as a covariate in the adjustment.
Methods: The parents of a large prospective birth cohort answered questionnaires on environmental factors and allergic symptoms when their children were 2 months and 1, 2 and 4 years old. Perinatal data on weight and length at birth were received from the child care health centres. The children were clinically examined at 4 years of age and height and weight recorded. Blood was drawn for analysis of specific IgE antibodies to common inhalant allergens. Risk associations between birth anthropometric measures and wheeze, allergic diseases or sensitisation were estimated in multivariate logistic regression analyses (n = 2869).
Results: There were no clear overall associations between birth weight and allergic diseases at 4 years of age. Birth length ⩾90th percentile was inversely associated with any wheeze at age 4 (adjusted OR 0.64, 95% CI 0.44 to 0.92) but was significantly associated only with late-onset wheeze (adjusted OR 0.40, 95% CI 0.21 to 0.77). No such associations were seen for persistent or transient wheeze, eczema, rhinitis or allergic sensitisation. Transient wheeze during the first 2 years of age tended to be associated with increased BMI at age 4.
Conclusion: Increased birth weight was not associated with wheeze or allergic disease. Increased birth length may play a protective role in late-onset wheeze in early childhood.

There has been a trend towards increased anthropometric measures at birth throughout the world in recent decades, particularly in more affluent countries.[1] Epidemiological studies have suggested that enhanced anthropometric measures at birth may be associated with asthma, other allergic diseases and sensitisation in children,[2–6] but so far data are not consistent and no firm conclusions can be drawn.[7] A recent comprehensive meta-analysis included nine cohort studies to estimate the effect of increased birth weight in childhood on the future risk of asthma.[8] Although the combined results from these nine studies had a pooled relative risk of 1.2 (95% CI 1.1 to 1.3) for increased birth weight on asthma, the original studies produced different results on this issue. In three studies, increased birth weight was shown to be a significant risk factor for diagnosed asthma, asthma hospitalisation and emergency visits.[9–11] However, in the other six studies, increased birth weight was not a significant predictor for asthma, with relative risk ranging from 0.9 to 1.5.[2 3 5 12–14] Birth length has been studied less than birth weight in terms of its effect on allergic disease. Birth length was not associated with asthma in most of the reports,[2 3 11 15] except for one study showing that increased birth length predicted asthma in children at 13 years of age.[5]

In addition, increased birth weight has been associated with a greater risk for being overweight in childhood.[16 17] A positive association between childhood overweight and asthma symptoms has been established.[18–23] Therefore, childhood overweight needs to be considered as a covariate for allergic outcomes and included in the adjusted risk assessment for enhanced anthropometric measures at birth and onset of allergic diseases. As this has not fully been studied in children, the aim of this study was to evaluate increased birth weight and birth length as key exposures in relation to wheeze, allergic symptoms and sensitisation at 4 years of age, taking childhood overweight in the adjustment as a covariate for wheeze and allergic symptoms.

METHODS

Subjects, questionnaires and clinical measurement

The studied population-based birth cohort consisted of 4089 infants (2065 boys and 2024 girls) born between February 1994 and November 1996 in central and north-western areas of Stockholm (BAMSE). Enrolment procedures and criteria for inclusion have been described in detail elsewhere.[24 25] Perinatal data including birth weight and birth length were received from the child care health centres. Data on environmental factors including maternal age, older siblings, parental smoking habits, parental employment and family history of allergy were collected from the parental questionnaires when the children were an average of 2 months old. When the children were 1, 2 and 4 years of age, questionnaires on symptoms related to asthma and other allergic diseases were distributed to the parents of all children.[26] At 4 years of age, an additional clinical examination was carried out, including blood sampling and recording of height and weight. All sera were analysed with Phadiatop, which contains a combination of the eight most common inhalant allergens (Pharmacia CAP System, Phadia AB, Uppsala, Sweden). For inclusion in this report, children had to meet the following two requirements: the parents had to have answered all the questionnaires at 2 months and at 1, 2 and 4 years of age (n = 3502, response rate 86%) and the children had to have participated in the clinical examination at age 4 (n = 2965, 73%). This resulted in 2869 (70%) children with complete data for analyses, of whom 2530 were analysed using Phadiatop.

Definition and classification of exposures and outcomes

Key exposures and covariates

Birth weight, birth length and body mass index (BMI) at 4 years of age were categorised into three groups based on the

Abbreviations: BMI, body mass index; CI, confidence interval; GA, gestational age; OR, odds ratio; SEI, socio-economic index

10th and 90th percentiles. The cut-off values and number of children in each category are given in table 1. There are no universally agreed definitions for high birth weight, high birth length or high BMI. We therefore chose birth weight ⩽10th percentile as being close to the clinical definition of low birth weight (birth weight <2500 g).[27] Moreover, BMI ⩾90th percentile was close to the cut-off values of overweight at 4 years of age derived from the International Obesity Task Force recommendations, that is 17.6 kg/m^2 for boys and 17.3 kg/m^2 for girls.[28] Birth weight, birth length and BMI were also categorised by quintiles.

Family history of allergy was defined as doctor-diagnosed asthma with asthma medication and/or rhinitis and/or pet or pollen allergy in at least one of the parents.[29] Young maternal age was defined as the mother being ⩽25 years of age at the birth of the index child. Exclusive breastfeeding was defined as the child being exclusively breastfed for 4 months or more. The presence of older siblings was defined as the child having at least one older sibling. Maternal perinatal smoking was defined as maternal smoking during pregnancy and/or during the first 2 months of life of the child. Socio-economic index (SEI) was classified according to the Nordic standard occupational classification and the Swedish socio-economic classification.[30 31] The children were categorised on the basis of their parents' occupation into unskilled and skilled blue-collar workers including students and the unemployed (as the reference category), low and intermediate level white-collar workers, and high level white-collar workers.

Wheeze and outcomes of allergic diseases

Any wheeze at age 4 was noted if the child had at least one episode of wheeze in the last 12 months at 4 years of age. Transient wheeze was defined as at least three episodes of wheeze between 3 months and 2 years of age, but no episode in the last 12 months at 4 years of age. Late-onset wheeze was defined as no episode of wheeze between 3 months and 2 years of age, but at least one episode in the last 12 months. Persistent wheeze was defined as at least one episode of wheeze between 3 months and 2 years of age, and at least one episode in the last 12 months.[29] Eczema at age 4 was noted if the parent reported that the child had an itchy rash for at least 2 weeks with typical distribution (face, outer limbs, folds of elbows/wrists, behind the knees, or fronts of ankles) and dry skin and/or a doctor's diagnosis of eczema between 2 and 4 years of age. Rhinitis at age 4 was noted if a runny or blocked nose without symptoms of having a cold in the last 12 months at 4 years of age was reported. Questions used to elicit information on wheeze, eczema and rhinitis closely followed the ISAAC criteria.[32] Sensitisation to airborne allergens was defined as a Phadiatop of ⩾0.35 kU/l.

Statistical analyses

All statistical analyses were performed with STATA 8.0 (College Station, TX, USA). Univariate and multivariate logistic regression models were used to analyse associations between key exposures (birth weight and birth length) and wheeze or allergic outcomes (wheeze between ages 2 and 4 and at age 4, and eczema, rhinitis and sensitisation at age 4). The results of univariate logistic regression analyses were presented as crude odds ratios (OR) with 95% confidence intervals (CI). Estimated risks of birth weight and birth length adjusted for each other were also calculated following adjustment for BMI at age 4 and other covariates, that is, family history of allergy, maternal age, gender, exclusive breastfeeding, presence of older siblings, gestational age, maternal smoking and SEI in final model. All these covariates were significantly associated with wheezing symptoms at age 4. The results of multivariate logistic regression analyses were presented as adjusted ORs. Interactions between gender and birth length ⩾90th percentile or BMI ⩾90th percentile in relation to wheeze over time were tested in a simple model without adjustment for covariates. To avoid false positive results in multiple testing, following adjustment for all covariates the significance level in the final model was set at $p<0.01$[33] and the tendency level at $p<0.05$. The study was approved by the ethics committee of Karolinska Institutet, Stockholm, Sweden.

RESULTS

In univariate logistic analyses, birth weight ⩾90th percentile was positively associated with BMI ⩾90th percentile at 4 years of age, male sex, ⩾1 older sibling and gestational age >42 weeks (table 2) but was not significantly associated with family history of allergy, young maternal age, exclusive breastfeeding or SEI. Birth length ⩾90th percentile was positively associated with male sex and gestational age >42 weeks but was not associated with other variables. Maternal smoking tended to be negatively associated with both birth weight ⩾90th percentile and birth length ⩾90th percentile.

Overall, no major associations between birth weight ⩾90th percentile and wheeze, allergic diseases or sensitisation at 4 years of age were found in crude analyses (tables 3 and 4) or following adjustment for birth length (data not shown). Additional adjustment for BMI at age 4 and the other covariates did not change the lack of association between birth weight ⩾90th percentile and wheeze or allergic diseases (tables 3 and 4). However, birth length ⩾90th percentile was inversely associated with any wheeze at 4 years of age, but only with late-onset wheeze in crude analysis (table 3) and after adjustment for birth weight (OR 0.64, 95% CI 0.44 to 0.92, $p = 0.014$ for any wheeze and OR 0.44, 95% CI 0.22 to 0.84, $p = 0.013$ for late-onset wheeze). Following further adjustment for BMI at age 4, the association of birth length ⩾90th

Table 1 Categories of birth weight, birth length and body mass index at 4 years of age

Minimum–maximum	Categories	Cut-off values	n	n (%)
Birth weight (537–5300 g)	⩽10th percentile	⩽2860 g	2869	288 (10.0)
	10th–90th percentile	>2860 to <4200 g		2289 (79.8)
	⩾90th percentile	⩾4200 g		292 (10.2)
Birth length (29–58 cm)	⩽10th percentile	⩽47 cm	2839	325 (11.4)
	10th–90th percentile	>47 to <53 cm		2100 (74.0)
	⩾90th percentile	⩾53 cm		414 (14.6)
Body mass index at age 4 (12.8–23.9 kg/m^2)	⩽10th percentile	⩽14.7 kg/m^2	2846	279 (9.8)
	10th–90th percentile	>14.7 to <18.0 kg/m^2		2294 (80.6)
	⩾90th percentile	⩾18.0 kg/m^2		273 (9.6)

Body mass index was calculated as body weight in kilograms divided by the square of the height in metres (kg/m^2). Some values for birth length (n = 30) and body mass index at age 4 (n = 23) are missing.

percentile and wheeze changed very slightly (OR 0.65, 95% CI 0.45 to 0.93, p = 0.018 for any wheeze and OR 0.42, 95% CI 0.22 to 0.83, p = 0.011 for late-onset wheeze).

In the final model of multivariate logistic regression following adjustment for birth weight, BMI at age 4 and the other covariates, birth length ⩾90th percentile still seemed inversely associated with any wheeze at age 4 (OR 0.64, 95% CI 0.44 to 0.92, p = 0.015) but was significantly associated only with late-onset wheeze (OR 0.40, 95% CI 0.21 to 0.77, p = 0.006) and not with persistent or transient wheeze (table 3). There was no significant difference between boys and girls in the association between birth length ⩾90th percentile and late-onset wheeze ($p_{interaction} = 0.34$). In addition, transient wheeze, that is, recurrent wheeze during the first 2 years of life, tended to be positively associated with BMI ⩾90th percentile at age 4 following adjustment for birth weight, birth length and the other covariates in the final model (OR 1.61, 95% CI 1.04 to 2.51, p = 0.033) (table 3). However, such association could not be demonstrated for any wheeze at 4 years of age, and there was no significant difference between boys and girls in the association between transient wheeze and BMI ⩾90th percentile ($p_{interaction} = 0.38$).

None of the anthropometric measurements were significantly associated with eczema, rhinitis or sensitisation at 4 years of age (table 4).

Similar associations for the development of allergic diseases were obtained when birth weight, birth length and BMI at 4 years of age were categorised by quintiles (data not shown).

DISCUSSION

To our knowledge, this is one of the few studies[34] to evaluate the relationship between increased anthropometric measures at birth and wheeze or allergic diseases in early childhood while taking childhood overweight into account. We found no evidence that childhood overweight plays an important role in the relationship between increased anthropometric measures at birth and allergic disease. In addition, we did not find any significant association between birth weight and wheeze or allergic diseases at 4 years of age. However, increased birth length was associated with reduced risk of wheezing symptoms, but not with transient or persistent wheeze, during the last 12 months at age 4. Furthermore, increased BMI at age 4 tended to be associated with wheezing only during the first 2 years of life and not at 4 years.

In support of our findings, previous studies showed no significant linkage between increased birth weight and asthma.[2 3 5 12–14] Rona *et al* showed that a larger ratio of length gain during the first year of life to birth length, as a reflection of smaller birth length for a given length gain, was positively associated with asthma symptoms.[35] Nevertheless, our findings should be interpreted with caution. Given the large number of comparisons performed, the results may have been due to multiple testing. To avoid false positive results, we set the significance level in the final model at $p<0.01$.

Our results differed from those of previous studies, in which increased birth weight was significantly associated with asthma in children at age 10–16,[9–11] atopic dermatitis at age 7[6] and hay fever at age 11–16 years.[4] The discrepancy between our results and these reports could be due to differences in sample size as the numbers in our study may be too small to demonstrate significance for a weak association. However, the fact that our study is prospective in nature may indicate that the predictive effect of birth weight on allergic disease is trivial. The age of the children when the study was conducted and the age when

Table 2 Birth weight or birth length ⩾90th percentile in relation to covariates in 2869 children in the BAMSE study

	Birth weight ⩾90th percentile		Birth length ⩾90th percentile	
	%	Crude OR (95% CI)	%	Crude OR (95% CI)
Body mass index (BMI) at age 4				
10th to 90th percentile	10.8	1.0	16.9	1.0
⩾90th percentile	21.5	2.25 (1.62 to 3.12)	17.1	1.02 (0.72 to 1.45)
Family history of allergy				
No	11.0	1.0	16.1	1.0
Yes	11.8	1.08 (0.84 to 1.38)	17.1	1.08 (0.87 to 1.33)
Young maternal age (⩽25 years)				
No	11.2	1.0	16.5	1.0
Yes	12.7	1.15 (0.74 to 1.79)	16.0	0.97 (0.64 to 1.45)
Sex				
Girl	8.9	1.0	12.4	1.0
Boy	13.6	1.60 (1.25 to 2.06)	20.2	1.79 (1.44 to 2.22)
Exclusive breastfeeding (⩾4 months)				
No	11.5	1.0	15.1	1.0
Yes	11.3	0.98 (0.71 to 1.35)	16.8	1.13 (0.85 to 1.51)
⩾1 older sibling				
No	9.3	1.0	15.5	1.0
Yes	14.0	1.59 (1.25 to 2.03)	17.8	1.18 (0.95 to 1.46)
Gestational age				
36 to 42 weeks	11.0	1.0	16.3	1.0
>42 weeks	22.9	2.40 (1.42 to 4.07)	24.4	1.65 (0.99 to 2.77)
Maternal perinatal smoking				
No	11.7	1.0	16.9	1.0
Yes	8.3	0.68 (0.45 to 1.03)	12.9	0.73 (0.51 to 1.03)
Socio-economic index				
Blue-collar	10.3	1.0	14.3	1.0
White-collar (low and intermediate level)	12.3	1.22 (0.86 to 1.73)	17.5	1.27 (0.93 to 1.74)
White-collar (high level)	10.7	1.04 (0.72 to 1.51)	16.3	1.16 (0.84 to 1.61)

10th percentile<birth weight<90th percentile and 10th percentile<birth length<90th percentile served as reference groups. CI, confidence interval; OR, odds ratio. Family history of allergy: doctor diagnosed asthma with asthma medication and/or rhinitis and/or pet or pollen allergy in at least one of the parents. Maternal perinatal smoking: maternal smoking during pregnancy and/or during the first 2 months of life of the child. Socio-economic index: classified according to the Nordic standard occupational classification and the Swedish socio-economic classification. The children were categorised on the basis of their parents' occupation into unskilled and skilled blue-collar workers including students and unemployed (as the reference category), low and intermediate level white-collar workers, and high level white-collar workers.

Table 3 Crude and adjusted odds ratios (OR) and 95% confidence intervals for the association between birth weight, birth length or body mass index at age 4 and asthmatic symptoms at 2 and 4 years in 2869 children (the BAMSE study)

	Any wheeze at 4 years, n = 454 (16%)			Transient wheeze, n = 222 (8%)			Late-onset wheeze, n = 169 (6%)			Persistent wheeze, n = 284 (10%)		
	n	Crude OR (95% CI)	Adjusted OR (95% CI)	n	Crude OR (95% CI)	Adjusted OR (95% CI)	n	Crude OR (95% CI)	Adjusted OR (95% CI)	n	Crude OR (95% CI)	Adjusted OR (95% CI)
Birth weight ⩽10th percentile, n = 288	65	1.65 (1.22 to 2.23)	1.39 (0.90 to 2.12)	28	1.50 (0.98 to 2.30)	1.24 (0.66 to 2.34)	23	1.57 (0.98 to 2.50)	1.35 (0.71 to 2.56)	42	1.82 (1.27 to 2.62)	1.47 (0.87 to 2.49)
Birth weight ⩾90th percentile, n = 292	46	1.06 (0.75 to 1.49)	1.19 (0.80 to 1.75)	25	1.18 (0.76 to 1.84)	0.94 (0.56 to 1.57)	13	0.78 (0.43 to 1.40)	1.17 (0.61 to 2.24)	33	1.26 (0.85 to 1.87)	1.18 (0.75 to 1.87)
Birth length ⩽10th percentile, n = 325	68	1.42 (1.06 to 1.91)	1.07 (0.71 to 1.60)	25	1.09 (0.70 to 1.70)	0.58 (0.30 to 1.10)	23	1.24 (0.78 to 1.97)	0.90 (0.48 to 1.68)	45	1.56 (1.10 to 2.22)	1.09 (0.66 to 1.78)
Birth length ⩾90th percentile, n = 414	48	0.70 (0.50 to 0.97)	0.64 (0.44 to 0.92)	35	1.07 (0.73 to 1.57)	1.02 (0.66 to 1.56)	12	0.45 (0.25 to 0.83)	0.40 (0.21 to 0.77)	36	0.88 (0.60 to 1.27)	0.82 (0.54 to 1.24)
BMI ⩽10th percentile, n = 279	50	1.19 (0.85 to 1.65)	1.11 (0.78 to 1.58)	23	1.17 (0.74 to 1.85)	1.12 (0.69 to 1.82)	22	1.39 (0.86 to 2.23)	1.38 (0.84 to 2.25)	28	1.09 (0.72 to 1.66)	0.97 (0.62 to 1.52)
BMI ⩾90th percentile, n = 273	44	1.04 (0.73 to 1.47)	1.05 (0.72 to 1.51)	28	1.46 (0.95 to 2.23)	1.61 (1.04 to 2.51)	10	0.65 (0.33 to 1.25)	0.73 (0.37 to 1.43)	34	1.36 (0.92 to 2.01)	1.35 (0.89 to 2.04)

BMI, body mass index at 4 years of age. The multivariate logistic regression models contained birth weight, birth length, BMI, family history of allergy, maternal age, sex, exclusive breastfeeding, presence of older siblings, gestational age, maternal smoking and socio-economic index.

allergic diseases manifest is another possible explanation for our results. We looked at a narrow age range during which asthma was less likely to be affected by other factors associated with birth weight compared to a wider age range. Besides, the discrepancy between our and previous reports could be explained covariates being treated differently in the adjustment. Childhood BMI has not previously been taken properly into account, but based on our results does not seem to be a significant factor in the association between birth anthropometric measurements and wheeze or allergic disease in this age group. Our finding of an inverse association between increased birth length and late-onset wheeze was somewhat novel, in contrast to a previous study in which increased birth length was positively associated with asthma in children at 13 years of age.[5]

In our study, wheezing symptoms were considered instead of a diagnosis of asthma by a doctor, since it is difficult to diagnose asthma in this age group; it has been proposed that the term asthma be replaced by wheeze and wheeze over time in small children.[29 36] Late-onset wheeze was more likely linked to atopy than transient or persistent wheeze. This was supported by the fact that there was a highly significant association between sensitisation to inhalant allergens and late-onset wheeze.[29] Our data may thus imply that increased

Table 4 Crude and adjusted odds ratios (OR) and 95% confidence intervals for the association between birth weight, birth length or body mass index at age 4 and allergic diseases or sensitisation at 4 years in 2869 children (the BAMSE study)

	Sensitisation at 4 years, n = 388 (15%)			Eczema at 4 years, n = 624 (22%)			Rhinitis at 4 years, n = 341 (12%)		
	n	Crude OR (95% CI)	Adjusted OR (95% CI)	n	Crude OR (95% CI)	Adjusted OR (95% CI)	n	Crude OR (95% CI)	Adjusted OR (95% CI)
Birth weight ⩽10th percentile, n = 288	37	0.92 (0.63 to 1.33)	1.06 (0.64 to 1.73)	56	0.86 (0.63 to 1.18)	0.98 (0.65 to 1.48)	35	1.05 (0.72 to 1.54)	1.25 (0.75 to 2.08)
Birth weight ⩾90th percentile, n = 292	32	0.79 (0.53 to 1.16)	0.66 (0.42 to 1.02)	66	1.05 (0.78 to 1.41)	0.99 (0.70 to 1.38)	37	1.09 (0.75 to 1.58)	1.17 (0.76 to 1.78)
Birth length ⩽10th percentile, n = 325	37	0.83 (0.57 to 1.21)	0.78 (0.48 to 1.25)	62	0.85 (0.63 to 1.14)	0.85 (0.58 to 1.24)	34	0.83 (0.56 to 1.22)	0.70 (0.42 to 1.16)
Birth length ⩾90th percentile, n = 414	63	1.15 (0.85 to 1.56)	1.22 (0.87 to 1.71)	94	1.06 (0.82 to 1.37)	1.05 (0.79 to 1.40)	45	0.86 (0.61 to 1.22)	0.84 (0.57 to 1.22)
BMI ⩽10th percentile, n = 279	32	0.79 (0.53 to 1.17)	0.87 (0.58 to 1.30)	53	0.83 (0.60 to 1.14)	0.84 (0.60 to 1.16)	41	1.31 (0.92 to 1.88)	1.37 (0.94 to 1.99)
BMI ⩾90th percentile, n = 273	25	0.64 (0.41 to 0.99)	0.71 (0.45 to 1.11)	61	1.02 (0.75 to 1.38)	0.99 (0.72 to 1.36)	27	0.83 (0.54 to 1.26)	0.82 (0.53 to 1.27)

BMI, body mass index at 4 years of age. Sensitisation to airborne allergens was defined as a positive Phadiatop (⩾0.35 kU/l). The multivariate logistic regression models contained birth weight, birth length, BMI, family history of allergy, maternal age, sex, exclusive breastfeeding, presence of older siblings, gestational age, maternal smoking and socio-economic index.

What is already known on this topic

- The trend of increasing anthropometric measures at birth in affluent counties has paralleled the increase in allergic diseases in children.
- Increased birth weight has been associated with an increased risk of childhood overweight.

What this study adds

- This is one of the few studies to evaluate the relationship between enhanced anthropometric measures at birth and wheeze or allergic diseases in children while taking childhood overweight into account.
- Increased birth length may play a protective role in the development of wheeze with late-onset in early childhood.

birth length plays a role in preventing the development of Th2-mediated asthma symptoms in early childhood. It is also possible that the preventive effect of increased birth length on wheeze is not immune-mediated since there is a lack of association between birth length and allergic sensitisation. Increased birth length is highly predictive of diminished airway resistance in healthy term neonates,[37] which may explain our results.

Although there are several prospective studies demonstrating increased BMI or obesity as a risk factor for the development of wheezing symptoms and asthma in children,[18 20 38–40] a causal relationship between obesity and asthma has yet to be elucidated.[41] Our study demonstrates a positive association between wheeze up to 2 years of age and BMI ⩾90th percentile at 4 years of age. Ponderal index (birth weight/birth length^3), which can be used as a marker of body fatness at birth, did not predict transient wheeze or any other outcomes in our study (data not shown). In support of our finding, wheezing during the first 3 years of life was associated with a greater risk of being overweight at age 5 in another birth cohort study (COAST).[42] Possible explanations for this are weight gain due to decreased activity in wheezing children or reduced gain in height due to medication. However, these hypotheses need to be examined in another setting. Meanwhile, our finding of an association between wheezing before age 2 and increased BMI at 4 years of age only shows as a tendency and needs to be interpreted with caution.

In summary, we were not able to demonstrate that increased birth weight or BMI at 4 years of age was associated with allergic disease at the same age. Increased birth length showed a decreased risk for wheeze at 4 years of age, but only for late-onset wheeze. If a similar result is found in future reports, further research should be carried out to determine its causes.

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Familial hemiplegic migraine with prolonged hemiplegia

Familial hemiplegic migraine (FHM), is rare, usually autosomal dominant, and characterised typically by attacks beginning with unilateral paraesthesia and weakness lasting for around 30–60 min, and followed by severe pulsatile, often contralateral, headache lasting for several hours. Three genetic subgroups have been identified, FHM1–3. FHM1 is due to mutations in the gene *CACNA1A* encoding a neuronal calcium channel subunit; FHM2 is due to mutations in the gene *ATP1A2* encoding a catalytic subunit of sodium potassium ATPase; and FHM3 is due to mutations in the gene *SCN1A* encoding a neuronal sodium channel subunit. In FHM1 there may be ataxia and interictal nystagmus. In FHM2 and FHM3 there may be seizures. Now three apparently unrelated children have been described who had prolonged hemiplegia (>1 week) and mutations in *ATP1A2* (J C Jen and colleagues. *Journal of Neurology, Neurosurgery, and Psychiatry* 2007;**78**:523–6). They were a boy aged 7 and two girls aged 9 and 10 years. All three had headache followed by hemiparesis lasting for between 1 week and 3 weeks. The episode was precipitated in one case by an illness diagnosed as viral gastroenteritis and in another by a minor head injury. The mother of one child and the father of another gave typical histories of hemiplegic migraine. Each of the children had a different missense mutation in *ATP1A2* and the two symptomatic parents had the same mutations as their children. None of the four unaffected parents had a mutation.

More than 20 different mutations in *ATP1A2* have been described in FHM2. Functional studies suggest that the mechanism causing FHM2 is loss of function in one sodium-potassium ATPase alpha 2 isoform gene.