ORIGINAL ARTICLES

Respiratory health in a total very low birthweight cohort and their classroom controls

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Abstract
Aims—To compare the respiratory health and function at 8 to 9 years of age of a total population based cohort of 300 very low birthweight (VLBW) children with that of two classroom controls (n=590) matched for age and sex.
Study design—Cohort study with controls.
Setting—Schools throughout Scotland.
Results—The VLBW children were more likely than their peers to use an inhaler, to be absent from school, and to be admitted to hospital because of respiratory illness. They were significantly shorter than their classroom controls, but even after adjusting for differences in height, the VLBW children had reduced forced vital capacity (FVC); this was associated with a history of prolonged ventilation (>28 days) and pneumothorax in the neonatal period. There were no significant differences between the groups in forced expiratory volume in one second (FEV_1)/FVC but twice as many (7·9% *v* 3·7%) of the VLBW children had ratios <70%, denoting obstructive airways disease. Poor expiratory function was associated with neonatal respiratory distress syndrome, prolonged ventilation, and the need for >40% oxygen. Exercise induced airway narrowing was increased in VLBW children (odds ratio=2·0; 95% confidence interval 1·2 to 3·4) and was very little changed by adjustment for inhaler use and exposure to cigarette smoke.
Conclusions—As in other low birthweight cohorts, respiratory morbidity was increased. Unlike previous studies, FVC was more affected than expiratory function in this VLBW population. Our findings support the hypothesis that poorer lung function is associated with very low birth weight, but not with intrauterine growth retardation.
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Keywords: lung function, respiratory morbidity, very low birth weight.

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Low birth weight has been implicated in the genesis of later respiratory morbidity in populations born some 40–50 years ago. Barker *et al*

in particular have suggested that poor lung function and death from chronic obstructive airways disease in adult life was associated with lower birth weight and weight at 1 year via the mechanism of poor lung growth.[1] Follow up studies of the increasing numbers of low birthweight infants now surviving provide an opportunity to investigate the association between birth weight and respiratory health in more recent cohorts.

Previous neonatal follow up studies have shown that the children who were at increased risk of respiratory morbidity were those who had respiratory support in the neonatal period.[2 3] Chan *et al*, however, found that low birthweight infants, irrespective of whether they had required ventilation in the neonatal period, had poorer respiratory function at 7 years than their classroom peers.[4 5] Others have shown that the increased hospital admission rates seen in very low birthweight (VLBW) populations compared with heavier children are associated mainly with admission for both upper and lower respiratory tract infections.[6–9] Chan *et al* reported that their low birthweight children (defined as those <2000 g) were of similar height to their peers by the age of 7 years and had similar forced vital capacity (FVC), but reduced forced expiratory volume in one second (FEV_1); this effect was worse for boys and where there was a history of maternal smoking.[4] In a large study of schoolchildren throughout the UK, Rona and his colleagues reported that birth weight for gestational age (that is, intrauterine growth) was significantly associated with FVC and FEV_1 after taking gestational age, parental smoking, and social factors into account.[10] In a large study of army recruits from Israel, Seidman *et al* found a significantly increased risk of asthma (after adjusting for ethnic origin, social class, paternal education, maternal age, and birth order) among those whose birth weight was below 2500 g.[11]

In contrast, Kitchen *et al* reported that in their very low birthweight population (born between 1977 and 1982) there was little evidence of impaired lung function at 8 years.[12] Changes in the management of neonatal respiratory disease over the past 10 years may be associated with these improvements in later lung function and the experience of an even more recent cohort is presented here.

The Scottish low birthweight study is a population based study of all infants liveborn in Scotland in 1984 who had birth weights less than 1750 g.[13] Those survivors who had birth weights less than 1500 g were reviewed at 8 to 9 years in school. This review provided the opportunity to investigate the respiratory function of a more recent cohort of VLBW children, to compare their performance with that of heavier birthweight children who lived in the same localities, and to test hypotheses about the relationship of low birth weight and intrauterine growth retardation to later lung function.

We knew that our cohort, unlike that of Chan et al, had been significantly shorter than reference populations at the age of 4·5 years.[13] We therefore expected to find that, compared with controls, the VLBW children would have smaller lungs and increased bronchial reactivity.

Methods
All 908 liveborn children born in Scotland in 1984, weighing less than 1750 g at birth, were eligible for entry into the study; of these 896 (99%) were enrolled. Maternal and perinatal data were collected by a research midwife and the children have been followed up at intervals since. At 8–9 years, a review was planned of those 341 children, weighing less than 1500 g who were still resident in Scotland. Their performance on a number of measures of growth, cognitive and neuromotor performance,[14] blood pressure, and respiratory function was compared with that of two classroom peers of the same sex, who were nearest in date of birth to the index child.

DATA COLLECTION
Permission for the study was given by the ethics committees of all health boards in Scotland and the directors of education in every region in Scotland. With the written permission of head teachers and parents, the children's respiratory function was assessed in school by four nurses trained in the study techniques.

MEASUREMENT OF GROWTH AND LUNG FUNCTION
The nurses were trained by an auxologist to measure height and weight using standard techniques recommended by the Child Growth Foundation.[15] After training by a respiratory technician, the nurses carried out tests of respiratory function, using a computerised pneumotachograph system (Compact, Vitalograph Ltd). FVC and FEV_1 were measured on three occasions; at baseline, and again at five and 10 minutes after five minutes of running exercise according to the protocol of Strachan.[16] The period of exercise took place in most settings within a school corridor or gymnasium, but on a few occasions had to be done outside because of pressure of space. Each measurement recorded was the best of three attempts (based on the greatest sum of FVC and FEV_1) achieved by the child, wearing a nose clip. The mean (SD) ambient temperature recorded at the time of lung function measurement was 21·0 (2·2)°C (minimum 15·0°C). Recordings were made at a later date if the child had had bronchodilators within the previous six hours.

Information about previous hospital admissions was obtained from parental questionnaire. Parents were also asked whether the child suffered from frequent coughs and colds, or had colds which required treatment from the general practitioner, or caused the child to be absent from school. In addition to this, parents were asked to report whether their child wheezed, whether this was with or without a cold, or after exercise, and whether there was a family history of asthma, bronchitis, or allergies. Parental questionnaires also supplied information on housing, including the presence of mould or dampness, as well as details of the child's exposure to tobacco smoke. No independent information on a formal diagnosis of asthma was available and so the use of an inhaler was taken as an indicator of doctor diagnosed asthma.

Perinatal data, abstracted from maternal and infant case records were available for the VLBW children. Four markers of respiratory health in the perinatal period were investigated for their association with lung function at 8–9 years; duration of artificial ventilation, duration of oxygen at levels more than 40%, the presence of the respiratory distress syndrome, and pneumothorax.

STATISTICAL ANALYSIS
For the majority of children, three measures of FVC and FEV_1 were available. The measures of FEV_1 depended on the relation to exercise in the protocol. Given practice in the procedure, FVC is unaffected by exercise and should remain constant and therefore, the maximum FVC recorded for each child was used to compare the two study groups.

Recently published British standards were used initially to obtain spirometric SD scores, corrected for height and sex, in order to compare the study groups.[17] The Scottish control children, however, had a larger FVC, on average, than the population used as standard. There was also evidence of a sex bias with the shift from the norms being more pronounced for our control girls (mean (SD) FVC SD score for boys was 0·24 (1·62) and for girls 0·44 (1·44)). The results for the VLBW children were therefore considered, more appropriately, relative to their classroom peers.

The relationship between height and FVC is known to have non-constant variance,[18] with increasing variability of FVC with increasing height, and this was present in our results. To remove the heteroscedasticity, natural logarithm (ln) transformations were made on both variables. These transformations had a negligible effect on the normality of the data. FVC was compared by an analysis of covariance, regressing ln(FVC) on ln(height) and adjusting

Table 1 Prevalence of factors associated with respiratory morbidity; values are number (%)

	VLBW (n=241)	Control (n=508)
Family history		
Bronchitis	46 (19)	97 (19)
Wheezing	42 (18)	90 (18)
Allergies	62 (26)	132 (26)
Housing		
Dampness	27 (11)	70 (14)
Mould	20 (8)	53 (11)
Exposure to smoking (cigarettes/day)		
Mother		
0	124 (53)	321 (65)
1–19	39 (17)	87 (18)
20+	73 (31)	89 (18)
All adults		
0	88 (37)	248 (49)
1–19	31 (13)	71 (14)
20+	119 (50)	186 (37)

for sex and case status to estimate the difference between VLBW and control children. Adjusted means were obtained from the model to remove the effect of height, and their confidence intervals (CIs) were calculated on the natural logarithm scale and transformed to obtain values for FVC in litres. Other important factors (age, current weight, social class, and exposure to tobacco smoke) were also explored in this model to establish their association with FVC and their effect on the difference between study groups.

FEV_1 is dependent on FVC, a factor found to differentiate the study groups. In order to compare VLBW and control children in respect of expiratory function, baseline FEV_1/FVC ratios were calculated. As the distribution of FEV_1/FVC was not normal, with the ratios being upwardly skewed toward unity, the non-parametric Wilcoxon rank sum test was used to compare FEV_1/FVC distributions. Ratios categorised by control centiles, were also used to investigate the difference between the two study populations in respect of airways obstruction. The prevalence of exercise induced airways narrowing (EIAN) was assessed by the number of children experiencing a 10% or more fall in FEV_1 after five minutes of free range running. The risk of EIAN in the VLBW population compared with the controls was estimated by the odds ratio (OR) with approximate CI and adjusted for confounding variables using logistic regression.[19] Proportions were compared by a χ^2 test of association and the risk of respiratory morbidity was again estimated by ORs with approximate CIs.

The methods used to compare cases and controls in respect of spirometric measures were also employed to test the associations between

perinatal factors and lung function in the VLBW population at 8–9 years. Duration of both artificial ventilation and the use of oxygen at levels more than 40% were not normally distributed and were therefore categorised as none, 1–6 days, 7–27 days, and ≥28 days in order to test for any dose-response relationship.

Results

Of the 341 VLBW children eligible for inclusion in this phase of the follow up, 324 (96%) were assessed at 8–9 years. Two children had been adopted and we were asked not to contact them, 11 parents refused further review, and four could not be traced. Only those children in mainstream education were included in the current analysis of respiratory function. This was due to the lack of appropriate controls for the 24 VLBW children in special schools and the fact that those children were unable to undertake the tests for reasons connected with their disabilities. Of the 300 VLBW and 590 control children assessed by the nurses, 292 and 574, respectively, provided at least the baseline measurement of FVC. All these children, except two VLBW cases, were also able to provide at least a baseline measurement of FEV_1. Reasons for missing data in this part of the study were largely due to equipment failure.

The mean age for both VLBW and control children was 8·8 years (case SD=0·3; control SD=0·4). The numbers of girls in each group were 153 (51%) and 298 (51%), respectively. The two groups of children differed greatly in height, with the control children closely resembling the distribution of the Child Growth Foundation's 1993 norms, while 14% (n=42) of the VLBW population had a height below the third centile for age and sex, and 76% (n=227) were below the 50th centile. Mean (SD) heights for cases and controls were 127·9 cm (6·0) and 131·4 (6·0) respectively.

Parental questionnaires were received, after a second mailing, from 241 (80%) VLBW and 508 (86%) control children, a significantly better response rate from the latter.

RESPIRATORY MORBIDITY AND ASSOCIATED FACTORS

Table 1 shows the proportions of children in each study group who were exposed to environmental factors associated with respiratory morbidity and who had a family history of respiratory disorders. The VLBW population did not differ significantly from the control children in respect of family history of bronchitis, wheezing or allergies, or in the presence of dampness or mould in the home. Current exposure to smoking was significantly more common in the VLBW children, both for exposure from the mother and additive exposure from all adults living with the child.

The VLBW population was found to have an increased risk of wheezing, both with and without a cold or after exercise. They also had more frequent coughs and colds (>5/year), and they were more likely to see their general practitioner because of this (table 2). They were more often

Table 2 Prevalence and risk of respiratory morbidity in the VLBW population

	No (%) VLBW (n=241)	No (%) control (n=508)	OR	95% CI
Wheeze				
Alone	22 (9)	23 (5)	2·1	1·2 to 3·9
With cold	56 (23)	67 (13)	2·0	1·3 to 3·0
After exercise	28 (12)	32 (6)	2·0	1·2 to 3·3
Frequent coughs and colds	55 (23)	52 (10)	2·6	1·7 to 3·9
Visited GP for coughs and colds	67 (28)	80 (16)	2·1	1·4 to 3·0
School absences for chest problems	31 (13)	24 (5)	3·0	1·7 to 5·2
Respiratory hospital admissions	40 (17)	23 (5)	4·3	2·5 to 7·4
Inhaler*	40 (13)	45 (8)	1·9	1·2 to 2·9

*Information from nurses' assessment, hence all children, excluding one VLBW child, responded. GP=general practitioner.
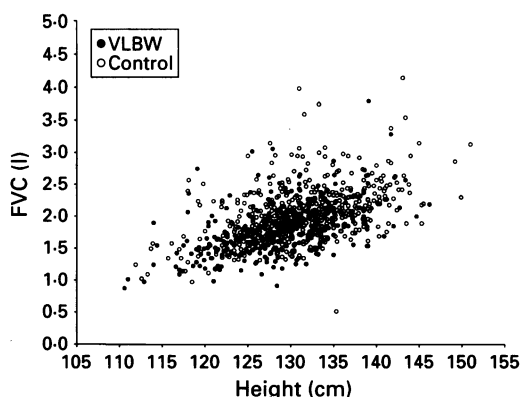
Figure 1   Association between FVC and height.

absent from school because of respiratory symptoms and were four times more likely to have been admitted to hospital on at least one occasion for respiratory problems (OR 4·3; 95% CI 2·5 to 7·4). Inhaler use was reported significantly more often in the VLBW population (13% *v* 8%: OR 1·9; 95% CI 1·2 to 2·9).

FORCED VITAL CAPACITY
As FVC depends strongly on height, and because the height of our VLBW population differed greatly from that of the controls, height was an important confounding variable. Figure 1 shows the maximum FVC plotted against height for both study groups; the 'fanning out' of the points with increasing values illustrates the non-constant variance characteristic of FVC. In fig 2 the mean FVC for height centile groups is plotted for each study group and illustrates a reduction at all heights for the VLBW population with the exception of those children with heights between the 50th and 75th centiles. An analysis of covariance, regressing ln(FVC) on ln(height) and correcting for sex, showed the FVC to be significantly reduced in the VLBW population (p<0·001); the difference between the study groups was the same for boys and girls. The slope of the regression between ln(FVC) and ln(height) was not significantly different between the study groups. Adjusted FVC means (95% CI), standardised to the mean height of the total study population (130·1 cm) were 1·81 litres (1·76 to 1·85) for the VLBW children compared with 1·91 litres (1·89 to 1·95) for their controls. Thus even
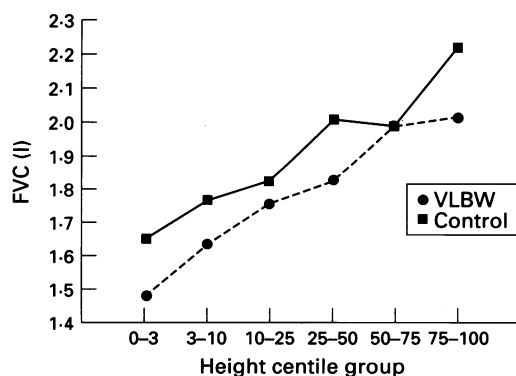

Figure 2   FVC by height centiles: VLBW children compared with controls.

after adjusting for their height, the VLBW children had a smaller FVC than the control children. Weight, but not age, was significantly related to FVC after adjusting for height. The additional variance explained by weight was, however, small (<1%) and had a negligible effect on the adjusted means. Social class, in four categories (I, II, and IIInm; IIIm; IV and V; other and missing) was also not significantly associated with FVC, after adjusting for height.

The effect of exposure to cigarette smoke on FVC was investigated in two stages; the additive exposure from all adults living with the child and exposure from the mother only; both variables were categorised as smoking or non-smoking. Additive exposure from all adults was not significantly associated with FVC; however, exposure from the mother alone was (p<0·05), although the effect was not as expected. In both study groups, the children exposed to maternal smoking had, on average, larger FVC than those not exposed, although these findings were not consistent with a dose-response relationship when the level of smoking was taken into account.

FORCED EXPIRATORY VOLUME IN ONE SECOND
Because of the reduction in FVC in the VLBW population, their FEV_1 measurements could not be compared with the controls without first adjusting for FVC. The distribution of FEV_1/FVC ratios for VLBW and control children were both skewed towards one (fig 3) with median ratios (interquartile range) being 0·88 (0·82–0·94) and 0·90 (0·84–0·94), respectively. A Wilcoxon rank sum test showed no significant differences in the distributions between the study groups. Airways obstruction is, however, characterised by low FEV_1/FVC ratios and in order to investigate this further, ratios were categorised into three groups, <0·70, 0·70–0·84, and 0·85+, corresponding respectively to below the 5th, 5th–25th, and above the 25th centile of the control population. A χ^2 test of association found this lower part of the FEV_1/FVC distribution to be significantly different between the study groups (p<0·05); the proportion of VLBW children who had ratios below 0·70 was twice that of the controls (n=23 *v* 22; 7·9% *v* 3·7%). After stratifying by sex, however, only the VLBW boys were significantly different from their controls.

Exposure to maternal smoking appeared to be related to a reduced expiratory function within the control group only; median FEV_1/FVC for control children, exposed and unexposed were respectively 0·88 and 0·91, while the median ratio for the VLBW children remained at 0·88 regardless of their exposure to maternal smoking. Wilcoxon rank sum tests confirmed that maternal smoking was significantly associated with a reduced expiratory volume in the control children only (p<0·01). Maternal smoking was not associated with evidence of obstructive airways disease (that is, FEV_1/FVC ratio <0·70) in either study group.
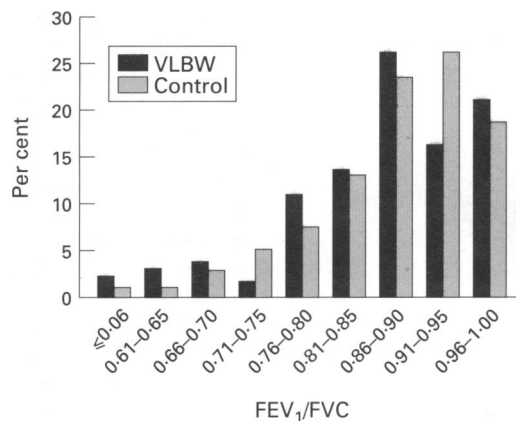
Figure 3 FEV₁/FVC ratio: VLBW children compared with controls.

EXERCISED INDUCED AIRWAYS NARROWING

A total of 30 (10%) VLBW and 31 (5%) control children experienced a 10% or more decrease in FEV_1 after the exercise period, a significantly increased prevalence of EIAN in the VLBW population (OR=2·0; 95% CI 1·2 to 3·4). EIAN has been shown to be increased in both children with asthma and in children exposed to maternal smoking,[20] and our low birthweight population had comparatively more in both these risk categories (table 1). To correct for these factors, logistic regression was carried out adjusting for whether or not the child was currently using an inhaler and whether or not the child's mother smoked. Adjusting for inhaler use, which was significantly associated with EIAN, the odds ratio for the VLBW population became 1·9 (95% CI 1·1 to 3·3). Adjusting for any smoking or heavy (>20/day) smoking resulted in a negligible increase in the odds ratio for the VLBW population. Maternal smoking was not significantly associated with EIAN for either VLBW or control children. The prevalence of EIAN was increased where parents reported that their child wheezed with a cold or after exercise.

PERINATAL FACTORS AND LUNG FUNCTION IN THE VLBW POPULATION

The four perinatal respiratory factors and their relationships to later lung function are sum-

marised in table 3. Analysis of covariance showed that both prolonged artificial ventilation (p<0·05) and the presence of pneumothorax (p<0·005) were significantly associated with a reduced FVC, with the decrease in FVC among children experiencing a pneumothorax remaining significant after adjustment for duration of ventilation. Only those children who were ventilated for 28 days or more had significantly reduced FVC compared with those who were not ventilated. Although birth weight and gestational age are inevitably related to the neonatal respiratory experience of the VLBW children, they were not themselves significantly related to FVC within the VLBW group. Poor expiratory function, defined as FEV_1/FVC less than 70%, was significantly associated with duration of artificial ventilation (p<0·05), prolonged use of oxygen at levels of 40% or more (p<0·005) as well as respiratory distress syndrome (p<0·01). Very few children without respiratory distress syndrome received artificial ventilation or prolonged oxygen; it was, therefore, not possible to establish the interdependence of the observed association between these perinatal factors.

The prevalence of EIAN was significantly increased in those children who had respiratory distress syndrome (OR=3·9; 95% CI 1·3 to 11·5) but was not significantly associated with any of the other perinatal variables.

Discussion

In this study, we have described the respiratory health and function in a geographically based cohort of Scottish VLBW children born in 1984. Most studies of longer term function have related to heterogeneous populations cared for in tertiary referral centres with many infants being transferred in for care because of severe respiratory problems and their populations are therefore likely to be biased.

The most striking finding in the present study was that lung size as measured by FVC was reduced in the VLBW population. After adjustment for height, the mean reduction in FVC was 110 ml in the VLBW infants. Moreover, expiratory function as measured by FEV_1/FVC was relatively well maintained in the VLBW children and, on average, their FEV_1/FVC was not reduced compared with the controls. The VLBW cohort did, however, have more children at the lower end of the distribution (fig 3), although the actual number in this category was small.

Our lung function findings are contrary to those of Chan et al where low birthweight children had maintained FVC and reduced FEV_1.[4] The most likely explanations for the differences in our results are that our cohort were of lower birth weight and were population based. Kitchen et al's study of VLBW children found little evidence of reduced respiratory function overall, although they did find that those children of extremely low birth weight (ELBW, <1000 g) had a reduced FVC compared with those with birth weights between 1000–1400 g.[12] We found no evi-

Table 3 Perinatal factors and respiratory function in the VLBW cohort at 8–9 years

		FVC		FEV₁/FVC		No (%)
	No	Mean*	95% CI	Median	No (%) <70%†	EIAN†
Artificial ventilation (days)						
None	134	1·84	1·77 to 1·91	0·90	4 (3)	11 (8)
1–6	66	1·83	1·73 to 1·93	0·89	7 (11)	7 (11)
7–27	57	1·83	1·73 to 1·94	0·87	7 (13)	6 (11)
28+	34	1·65	1·52 to 1·78	0·86	5 (15)	6 (18)
Oxygen ≥40% (days)						
None	109	1·81	1·73 to 1·88	0·89	2 (2)	10 (9)
1–6	125	1·83	1·75 to 1·91	0·89	11 (9)	14 (11)
7–27	37	1·80	1·69 to 1·92	0·86	6 (16)	3 (8)
28+	21	1·78	1·61 to 1·97	0·86	4 (20)	3 (15)
Respiratory distress syndrome						
No	102	1·81	1·73 to 1·89	0·89	2 (2)	4 (4)
Yes	190	1·81	1·75 to 1·88	0·88	21 (11)	26 (14)
Pneumothorax						
No	272	1·83	1·78 to 1·89	0·89	21 (8)	28 (10)
Yes	20	1·57	1·44 to 1·72	0·88	2 (10)	2 (10)

*Adjusted for height and sex in analysis of covariance for VLBW cohort only, to a height of 130·1 cm. †x^2 test for association between FEV_1/FVC <70% and EIAN with duration of artificial ventilation and oxygen ≥40% performed combining the middle categories of explanatory variables (none, 1–27 days, and 28+ days) because of small numbers.

dence of differential lung function for the ELBW children in the Scottish cohort. It may be noted, however, the Kitchen *et al* used published standards to obtain the percentage of predicted scores for lung function measures and our own experience of published norms was not favourable. Had we not included a control group in our study we would have reached different conclusions about the lung function of the VLBW cohort, highlighting the importance of control groups for epidemiological studies even when very recent norms are available.

As in earlier reports,[5][12] we found that VLBW children had evidence of significant respiratory morbidity, particularly wheezing illnesses, compared with their classroom peers. Kitchen *et al* found increased levels of asthma and recurrent bronchitis which were associated with reduced flow rates.[12] A number of studies have reported that respiratory symptoms are significantly associated with length of gestation, whereas lung function is related to birth weight. For example, Kelly *et al* stated that preterm birth *per se*, but not intrauterine growth retardation, predisposed to the later development of asthma.[21] Rona *et al* found that every additional week of gestation reduced the risk of severe wheeze by about 10%, independently of birth weight, while birth weight for gestation was significantly associated with lung function measures.[10] Others, however, reporting on lung function in adolescents (born in 1975–7), reported that low birth weight at term (that is intrauterine growth retardation) was not associated with reduced lung function.[22] Of the 300 VLBW infants in our study, 94 (34%) were also small for gestational age. These infants did not have either a reduced FVC or a poorer FEV_1/FVC ratio than appropriately grown VLBW children. Thus, we also cannot confirm the association of obstructive airways disease with intrauterine growth retardation reported by Barker and colleagues.[1] We acknowledge, however, that our study was not ideal to investigate such a hypothesis because the cohort was defined by birth weight and not also by gestational age.

Some of our findings in respect of exposure to smoking are unexpected but our intention in this paper was to focus on the effects of being very low birth weight on respiratory function rather than on known associations between smoking and respiratory function. In the control population, we found the expected association between FEV_1/FVC and exposure to passive smoking, but in the VLBW population no such relationship existed. In both populations, the FVC of children exposed to smoking was greater than in those not exposed, although the effect was small and there was no evidence of a dose-response relationship when the level of smoking was taken into account.

Our data on smoking exposure were derived from parental questionnaires from cases and controls and are, therefore, subject to all the usual biases in self reporting of such behaviour. There was also a significant difference in questionnaire response between these two groups with the VLBW group responding less fre-

quently (80% *v* 88%). However, the lung function of the children of non-responding parents was not significantly different from those who did respond; therefore response bias does not account for our findings. Furthermore, mother's smoking behaviour recorded at the time of birth correlated highly (88%) with data on exposure to maternal smoking at 8–9 years. It is not possible, therefore, to clarify whether our observed smoking effect is attributable to smoking in pregnancy or current exposure or both.

We did not find a difference between the two groups in the reporting of dampness and moulds in the house, nor was there a significant relationship between their presence and measures of lung function, as has been reported previously.[23] Where parents reported dampness and moulds in the home, they were also more likely to say that their child wheezed with a cold, irrespective of the study group. Wheezing in the absence of infection was increased only in the control children in association with reports of dampness and moulds. Other studies have also reported a strong and consistent relation between measures of home dampness and respiratory symptoms in children.[24]

Although in almost all respects, the VLBW children in this study had more respiratory problems than did their controls, these data showed that for the majority lung function was not as badly affected as we had expected. It would be informative to reassess these children's lung function in adolescence to ascertain whether there are improvements with maturation. Meanwhile these data provide a baseline for the respiratory outcomes of neonatal care for VLBW infants before the important recent advances such as the more frequent use of antenatal steroids in preterm labour and the introduction of surfactant treatment occurred.

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High evolutionary theory

Like the human lemmings who repeatedly, and apparently voluntarily, fling themselves (in caudocephalic orientation if fortune favours them) down perilous icy mountain slopes, their feet bound to slats of painted wood or some convenient modern substitute, primitive man must have been possessed of a self destructive urge. How else would you explain the fact that 25,000 years ago people took up residence high in the Himalayas, on the Tibetan plateau at 12,000 feet or more above sea level? For that, we are told, is the length of time the ancestors of present day Tibetans have been there. The vagaries of man's behaviour in the region did not, however, end there, for as we all know, some 45 years ago the Tibetans' northern neighbours decided to move in from China. And that has provided the basis of an interesting observation on darwinian natural selection (Susan Niermeyer and colleagues, *New England Journal of Medicine* 1995; **333**: 1248–52).

Fifteen Tibetan and 15 Han Chinese normal term babies in Lhasa were studied with serial pulse oximetry over the first few months of life. The Tibetan babies had higher arterial oxygen saturations from birth. The values in both groups fell during the first week after which in the Tibetan babies mean oxygen saturation stayed at around 86 to 90% but in the Han babies it fell progressively, reaching 76 to 78% in sleep at 4 months. Almost all of the Han babies were cyanosed during sleep. It is known that some Han babies fail to thrive in Lhasa and have to be taken to low altitude and some suffer from subacute infantile mountain sickness (they develop dyspnoea and cyanosis with pulmonary hypertension and right heart failure).

The precise physiological mechanisms underlying these observations are unknown. These authors suggest that there might be a genetic difference in the response of the pulmonary vasculature to hypoxia, the Tibetan babies being more resistant to the development of pulmonary hypertension.

There must be a moral in this story, about nation's behaviour unto nation, but I struggle to put it into words without appearing to condone that most unpaediatric principle about the sins of the fathers.

ARCHIVIST