nature of this activity is verified from the time-position information at the time of recording. The simultaneous recording of velocity with position of the chest wall gives further help in analysing fetal respiratory movement.

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Follow-up study of small-for-dates babies

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Summary

A group of small-for-dates full-term babies whose intra-uterine growth was followed by serial ultrasonic cephalometry were examined at a mean age of 4 years. Those children whose skull growth had begun to slow in utero before 34 weeks' menstrual age were more likely to have a height and weight less than the 10th centile. When the onset of growth failure had occurred before 26 weeks there was a lower developmental quotient at follow-up using the Griffiths extended scales. Prolonged slow growth in utero therefore seems to be followed by slow growth and development after birth.

Introduction

Small-for-dates babies are more likely to die at birth than normal babies, and follow-up studies show that some of these children continue to grow poorly.¹⁻⁶ They may also have an increased incidence of mental handicap, and a significant number have educational difficulties.⁷⁻⁸ It has not been possible, however, to predict at birth which small-for-dates babies will continue to grow slowly or have learning difficulties, even if their birthweight is 40% under the expected value.³

We thought that the intrauterine growth pattern and rate might help in this prediction and we therefore assessed 60 small-for-dates term babies when they reached about 4 years of age. The antenatal growth of all these babies had been followed by serial ultrasonic cephalometry.

Patients

Records were found of 93 babies who were small for dates at birth and who had had adequate serial cephalometry. Sixty children were traced and seen for follow-up examination. A further 21 children were traced, but could not be seen (12 had emigrated, three refused to attend, four had been adopted, and two had died). Three children were excluded as they had a condition which might cause poor growth—major congenital abnormality, chromosomal abnormality, or congenital viral infection. The remainder could not be traced. All but four of the children were Caucasian; all were singleton births.

The standards used for classifying the birth weights into centile groups allow for maternal height and weight and the baby's sex.⁹ A baby was called small for dates if the birth weight was below the 10th centile. Menstrual age was calculated from the mother's last menstrual period and confirmed by early biparietal diameter measurement (BPD); in five cases, when maternal dates were not certain, the expected date of delivery was calculated from early cephalometry alone.¹⁰ All babies were born at term—that is, the menstrual age was 37 or more completed weeks. Paediatric examination agreed with the period of gestation in all cases.

Fifty-four of the babies were born at Queen Charlotte's Maternity Hospital; the remaining six were born at five different hospitals in the UK. All had standard neonatal care, including resuscitation, early feeding, attention to temperature control, and the detection of hypoglycaemia.

ULTRASOUND INFORMATION

In most cases the mother had been referred to the ultrasound department because the fetus was thought to be small on abdominal palpation. Serial measurements of BPD were begun on all patients before 30 weeks' menstrual age and were continued to within two weeks of delivery. The technique of cephalometry has been described,¹¹ and all the measurements were made by SC. The reproducibility of measurements is high (the 95% confidence limits for weekly growth

FIG 1—Cephalometry growth chart showing growth of fetal biparietal diameter with late slowing. Labour was induced at 38 weeks because of pre-eclampsia; emergency caesarean section was performed for fetal distress and the Apgar score was two at one minute. Birth weight was 2450 g.

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being ± 0.71 mm), thus making weekly estimates of fetal growth a meaningful exercise.¹²

The severity and time of onset of slow growth was assessed by comparing the recorded BPD values with the normal graphs of Campbell and Newman.¹³ Slow growth was defined as a weekly increment in the size of the BPD falling below the 5th centile limit over two weeks or more. The time of onset of growth failure was determined on the graph of the normal range by establishing the point at which the fetal growth line deviated from the normal. When slow growth was of short duration the onset was usually clearly defined (fig 1). In cases of prolonged growth failure slowing of head growth often occurred before the first ultrasonic measurement had been made, and the recorded fetal growth line was extrapolated backwards to the mean (fig 2) to establish the time of onset of growth failure. The extrapolation line in some cases may have underestimated the duration of growth retardation, but we believe that in all cases the minimum period of growth failure of the fetal BPD was obtained.

FIG 2—Cephalometry growth chart showing prolonged slow growth of fetal biparietal diameter; growth line has been extrapolated backwards to median (broken line), which indicates that onset of growth failure was at 17 weeks menstrual age. Labour was induced at term; there was no intrapartum asphyxia and birth weight was 1890 g. Paediatric examination suggested that the baby was neurologically mature.

With this information on antenatal growth the 60 small-for-dates babies were grouped for analysis according to the time of onset of growth failure in utero. Group 1 comprised 13 babies whose growth failure had started at or before 26 completed weeks of gestation. Group 2 comprised 18 babies whose growth failure had started after 26 weeks but at or before 34 weeks of gestation. Group 3 comprised 10 babies whose growth failure had started after 34 completed weeks of gestation. Group 4 comprised 19 babies who had had no cephalometric evidence of growth failure.

Methods

All children were examined by one examiner (RF) who had no knowledge of the ultrasound information or the perinatal history. The mean age at follow-up was 4.0 years (range 28–84 months). There were 23 boys and 37 girls. Various investigations were carried out on each child.

History—Perinatal history and obstetric details were taken from the case notes. A medical and family history and developmental milestones were obtained from the mother; general practitioners were asked for any important medical or social history. The height of both parents was also noted.

Anthropometry—Height (or supine length to the age of 3 years), weight, head circumference, and subscapular and triceps skinfold thicknesses were all measured using standard equipment and techniques.¹⁴ As the anthropometric data was cross-sectional, the measurements were converted to centiles taking account of age, sex, and mid-parental height.^{15–18} In this way centiles could be compared irrespective of the age of the child.

Developmental quotient—The Griffiths extended scales¹⁹ were used to assess development in six areas: locomotion; personal-social; hearing and speech; eye and hand co-ordination; performance; and practical reasoning. Assessment was possible in 57 children. Of the remainder one spoke no English, another had bilateral cataracts, and the third was too shy to allow accurate testing.

Results

Height—The height centiles of the children were skewed to the right in those who had grown slowly in utero at or before 34 weeks (groups 1 and 2). In contrast, height centiles were distributed normally in children in groups 3 and 4. This difference in distribution was significant ($\chi^2 = 18.95$, $P < 0.0005$) (see table). The numbers of very short children in each group were compared by selecting those with a height on or below the 10th centile. There were significantly more short children in groups 1 and 2 (17 out of 31 children, compared with six out of 29 in groups 3 and 4; $\chi^2 = 6.02$, $P < 0.025$). We matched 18 children from groups 1 and 2 for age (within six months), sex, and social class with 18 from groups 3 and 4 in an attempt to exclude some factors that might influence postnatal growth. The difference in height centiles between the pairs was highly significant. Those with earlier growth failure were more likely to be short (distribution of height centiles between matched pairs: $\chi^2 = 17.44$, $P < 0.0005$; with height centile < 10 th in matched pairs: $\chi^2 = 4.33$, $P < 0.05$). Analysis of mid-parental height showed no significant differences among the four groups.

Weight—Weight centiles were similarly skewed to the right in groups 1 and 2 compared with groups 3 and 4 ($\chi^2 = 12.46$, $P < 0.01$) (see table). Groups 1 and 2 also contained significantly more children whose weight was on or below the 10th centile at follow-up. Eighteen of the 31 children in groups 1 and 2 were very light compared with six of the 29 in groups 3 and 4 ($\chi^2 = 7.23$, $P < 0.01$). The 18 children from groups 1 and 2 who were matched with the 18 from groups 3 and 4 were further analysed. Those with earlier slow growth in utero were lighter at follow-up (distribution: $\chi^2 = 14.65$, $P < 0.001$; weight < 10 th centile: $\chi^2 = 10.13$, $P < 0.005$).

Head circumference—The distribution of head circumference centiles was also skewed to the right in groups 1 and 2 ($\chi^2 = 6.85$, $P < 0.05$) (see table). Analysis of the number with a head circumference on or below the 10th centile at follow-up showed no difference between the groups. Significantly more children in groups 1 and 2, however, had a head circumference on or less than the 25th centile (28 out of 31 children in groups 1 and 2; 15 out of 29 children in groups 3 and 4; $\chi^2 = 10.69$, $P < 0.005$). The 18 matched pairs showed a significant difference in the number with a head circumference on or below the 10th centile ($\chi^2 = 4.33$, $P < 0.05$).

Skinfold thickness—There were no significant differences in skinfold thicknesses between the four groups.

Developmental quotient—Those children whose growth failure was very early (group 1) had a mean development quotient ($\pm$ SD) of 93.3 ± 8.05 compared with a mean quotient of 102.0 ± 10.86 for all other groups ($t = 2.40$, $P < 0.02$). The scores were normally distributed in all groups. The four subscales which were free from bias on the basis of any behaviour reported by the mother, rather than observed, were those of eye and hand co-ordination, hearing and

Height, weight, and head circumference centiles of children at follow-up examination.

Centile:					Height			Weight			Head circumference		
					<10th	10–50th	–90th	<10th	10–50th	–90th	<10th	10–50th	–90th
Groups 1 and 2	..	..	..	..	14	17		17	9	5	15	12	4
Groups 3 and 4	..	..	..	..	2	17	10	4	11	14	5	16	8

speech, performance, and practical reasoning. If these four were considered alone the resulting score was also significantly lower in group 1 ($t=4.07$, $P<0.001$). The differences in individual sub-quotients were: practical reasoning $P<0.01$; eye and hand co-ordination $P<0.01$; motor development $P<0.01$; and personal-social factors $P<0.05$. Mean scores on the hearing and speech and performance scales, taken individually, were not statistically different although both were lower in group 1.

OTHER FACTORS

Age—There were no significant differences between the four groups in age at follow-up.

Social class—The social class of the children was classified according to the father's occupation using the Registrar General's classification. Forty-two of the families belonged to social classes II or III. There was no difference in social class distribution between the four groups.

Obstetric and perinatal factors—No differences were found in maternal age or parity between the four groups nor in the incidence of pre-eclamptic toxæmia or hypertension in the pregnancy. Analysis of the incidence of birth asphyxia (as shown by a low Apgar score), serum bilirubin concentration of 205 $\mu\text{mol/l}$ (12 mg/100 ml) or greater, respiratory problems, minor congenital defects, neonatal or later convulsions, and major infections showed no differences between the groups. There was only one case of asymptomatic hypoglycaemia among the 60 babies. This child was in group 3; she had a concurrent septicaemia and required intravenous dextrose for 48 hours.

Discussion

We have described poor postnatal growth in those small-for-dates babies who had prolonged poor antenatal growth. Follow-up reports have also shown that a significant number of small-for-dates infants remain small.³⁻⁶ Their head circumference centiles have also been reported to be skewed to the right.^{2,10} Although it has been shown that a small-for-dates baby is more likely to grow slowly in childhood, up to now there has been no way of telling at birth which children will remain small and which may later catch up in growth.

Ultrasonic cephalometry is now a standard method of measuring the growth of the fetus in utero. This technique probably reveals particularly severe growth failure because brain growth is thought to be less affected than the growth of other organs in the malnourished fetus.²¹ Our results indicate that growth failure severe enough to be shown by this method may be continued into childhood if the process begins at or before the 34th week of menstrual age in a pregnancy that proceeds to term. This technique of measuring fetal growth is therefore a good way of predicting growth failure in childhood. The more recent method of ultrasonic measurement of the abdominal circumference may be even more valuable in making a prognosis for later growth.¹⁰

It has been shown that stunting of final mature size by undernutrition at a critical period of maximum growth velocity occurs in laboratory animals.²² This permanent stunting is associated with a deficit in final cell numbers in the organs of such animals.²³ A similar finding has been reported in cell numbers, based on estimation of total DNA, in small-for-dates human fetuses.²⁴ The short children in our study may have a similar loss of total numbers of cells.

Somatic growth, as well as later developmental and intellectual ability, may be altered by many subtle influences, nutritional and non-nutritional, postnatally. We were unable to take account of many of these but can say only that race, social class, and perinatal and medical histories of the children showed no major differences between any of the groups. That slow intra-uterine growth is related to stunting of height and weight and, to a lesser extent, head circumference is supported by two other studies. One is a report on twin pairs where the smaller baby had a deficit of at least 25% in body weight compared with his twin. The smaller child at birth remained at a disadvantage in

height, weight, head circumference, and later intellectual ability.²⁵ The other study was a community survey which showed that low birthweight continued to affect later height and intellect despite the variation imposed by social class.⁴

Those children who were already growing slowly before 26 weeks had a lower developmental quotient at follow-up. The assessment of developmental skills cannot reliably predict future intelligence, but Griffiths did report high correlations between a general quotient on her scale and the score on a Stanford-Binet test when both tests were carried out at the same time.¹⁹ If the retardation of developmental skills we have reported is accompanied by poor intellectual ability (either as measured by an intelligence test or as shown by poor school performance) then it is obviously very important. Follow-up studies of small-for-dates infants certainly indicate that they are likely to fail in school,⁷ and that they may have a lower intelligence quotient,^{4, 8, 26} but again it has been impossible at birth to predict which children are at risk. We do not know what has caused the poor intellect of these children, but as the slow growth occurred towards the end of the second trimester it may have interfered with the neuroblast proliferation between 12 and 18 weeks.²⁷

We intend to continue this study to include longitudinal information on growth and to follow these children into school age in an attempt to answer some of the important questions raised.

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