Should infants be screened for anaemia? A prospective study investigating the relation between haemoglobin at 8, 12, and 18 months and development at 18 months

A Sherriff, A Emond, J C Bell, J Golding, and the ALSPAC Study Team

Abstract

***Aims*—To investigate the relation between haemoglobin in children followed longitudinally from 8 to 18 months, and developmental outcome at 18 months.**

***Methods*—The Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) is a longitudinal survey of a geographically defined population of children born in 1991–92. In a randomly selected subsample, blood samples were assayed for Hb at 8, 12, and 18 months; a developmental assessment was carried out at 18 months on 1141 children using the Griffiths Scales of Mental Development.**

***Results*—There was a strong quadratic association between Hb at 8 months and performance on the locomotor subscale at 18 months. Average scores increased with increasing Hb up to 95 g/l; there was little additional developmental benefit in Hb levels beyond 95 g/l. Infants with Hb <95 g/l at 8 months of age scored on average 6 points lower on the locomotor subscale than infants with Hb ⩾ 95 g/l; infants with Hb <90 g/l at 8 months scored 12 points lower on the locomotor subscale than children with Hb ⩾ 90 g/l.**

***Conclusions*—Low Hb concentrations (⩽ 95 g/l) in 8 month old children are associated with impaired motor development at 18 months. This cut off point corresponds to the 5th centile of Hb at 8 months. The results indicate that if there is an adverse effect of low Hb on developmental outcome, screening may be more effective at 8 months or earlier, rather than after this age. We propose to examine the importance of infant anaemia in relation to more accurate and detailed long term outcomes as the children get older.**

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Iron deficiency anaemia is the most common nutritional deficiency in the developed world and is a particular problem in preschool children living in inner city areas.[1] Estimates of the prevalence of anaemia in infants varies between 12% and 30% according to the population studied[2] and the cut off used to define anaemia.[3]

The evidence associating iron deficiency anaemia with poor developmental outcome in children is mounting. A number of studies carried out both in developing countries,[4–6] and in Britain[7] have shown that varying degrees of anaemia in young children are associated with poor cognitive and non-cognitive outcomes. Although under some circumstances iron supplementation has been shown to partially reverse the damage,[8–11] a general consensus has yet to be reached on causation, as the relation between anaemia and development is complicated by multiple confounding variables. A number of animal studies have shown physical and functional effects of poor nutrition on the developing brain, particularly affecting arousal and reactivity.[12] The brain of the iron deficient rat shows impaired myelination, and altered neurotransmitter function, particularly if the iron deficiency exists during the brain growth spurt between 10 and 28 days of life. Results from a recent study suggest that a chronic marginal iron deficiency during the pre- and postnatal development of mice can result in functional changes in motor development, even in the absence of iron deficiency anaemia.[13]

Although studies of early diet in humans have shown negative effects of poor nutrition on developmental outcome later in childhood,[14] there is little evidence to implicate iron deficiency in the absence of anaemia with subsequent developmental impairments.[15] Questions as to whether a critical period of vulnerability to iron deficiency exists during the human brain growth spurt, and what degree of anaemia caused by iron deficiency is needed to impair development, have yet to be satisfactorily answered.

This study examines the relation between haemoglobin concentrations at 8, 12, and 18 months of age and subsequent developmental outcome at 18 months. Specifically, we explore whether a critical period of vulnerability to anaemia exists in the first 18 months and if so, what degree of anaemia is required to observe impaired development.

Methods

STUDY SAMPLE

All births in the former Avon Health Authority area with an expected date of delivery between 1 April 1991 and 31 December 1992 were eligible for the Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC). Over 80% of the known births from the geographically

defined catchment area were included, resulting in a total cohort of 14 138 surviving live births. From the population cohort, a 10% sample of randomly selected parents whose babies were born within the last six months of the survey were invited to bring their children to a research clinic (Children in Focus) at 4, 8, and 12 months of age and six monthly intervals thereafter, where a number of clinical, physiological, and developmental assessments were carried out. For this study, data were obtained from infants attending the 8, 12, and 18 months clinics. Of those invited, 1312 (83%), 1241 (89%), and 1181 (86%) children attended the clinics at 8, 12, and 18 months old respectively. The mean ages of children attending the 8, 12, and 18 month clinics were 35, 54, and 80 weeks old, respectively.

BLOOD ASSAYS

A heel prick sample of capillary blood was taken from the children and collected into an EDTA capillary tube. The haemoglobin concentration was assayed using the HEMOCUE B-Hb photometer. The quality assurance scheme operating within the laboratory and the measures taken to test the stability of the samples have been reported previously.[16]

DEVELOPMENTAL ASSESSMENTS

Development at 18 months of age was assessed using the Griffiths Scales of Mental Development.[17] Because of time constraints imposed by the clinic setting, children were assessed using year 2 of the scales only. The Griffith's battery has five subscales: locomotor, hearing and speech, hand/eye, performance, and social/personal. The scores produced were age adjusted and then averaged to form an individual developmental quotient (DQ). Eight qualified staff, blind to the haemoglobin status of the children at each time point, tested a total of 1141 children aged 18 months. It was found on examination of the intertester reliability that one tester scored higher than all the others. As a consequence, in all analyses, the tester effect was adjusted for. Additional data collected at the time of testing included the child's demeanour, the carer's impression of the child's performance, and the tester's own perception of the child's performance.

POSSIBLE CONFOUNDERS

A number of variables were included in the analyses as potential confounders of the relation between haemoglobin concentrations and developmental outcome. These were maternal parity/or number of previous pregnancies resulting in a live or still birth (0, 1, 2+), gender (male, female), ethnicity (white, non-white), whether the child was breast fed in the first six months (yes, no), whether the study mother smoked during pregnancy (yes, no), and highest maternal educational qualification (five point scale: A lowest, E highest). These variables were gathered prospectively from self report questionnaires completed by the study mothers at regular intervals throughout the study period.

ETHICAL APPROVAL

Ethical approval for the study was obtained from the ALSPAC ethics committee, and the local ethics committees of United Bristol, Southmead, and Frenchay Health Care Trusts. Following their advice, the results of those children whose haemoglobin was found to be less than 80 g/l were given to the mothers, with a letter to hand to their general practitioner suggesting further investigation.

STATISTICAL ANALYSES

All statistical analyses were carried out using SPSS for Windows (version 7.5.1). Univariable associations between haemoglobin concentrations and developmental outcome and the confounding variables were tested using one way analysis of variance (ANOVA) or independent sample *t* tests. Generalised linear modelling (GLM) techniques were used to model the relation between developmental outcome and haemoglobin concentrations at 8, 12, and 18 months of age respectively. Both linear and quadratic terms for haemoglobin were offered to the models, and adjustments were made for the confounding factors.

To determine the level(s) of anaemia associated with impaired development in this sample of children, haemoglobin concentrations were grouped into intervals of 5 g/l ranging from 70 g/l to 110 g/l with a final group containing all Hb > 110 g/l. The first three groups had to be combined owing to the small numbers occurring in each group, and three children with exceptionally high haemoglobin concentrations (Hb = 150 g/l) were also separately grouped. ANOVA models were used to assess whether there were statistical differences in average performance between haemoglobin categories after adjusting for all possible confounding variables.

Results

In total, 1141 children were assessed at 18 months of age using year 2 scores from the Griffiths Scales of Mental Development. Of these, 918, 815, and 788 had sufficient volume of blood for haemoglobin assay at 8, 12, and 18 months of age respectively.

Table 1 presents descriptive statistics for haemoglobin concentrations in our sample of children at 8, 12 and 18 months respectively, and table 2 presents statistics for the five subscales and developmental quotient of the Griffiths test at 18 months. Mean (SD) haemoglobin concentrations and Griffiths scores for the confounding factors are also presented along with appropriate p values.

HAEMOGLOBIN CONCENTRATIONS

Mean haemoglobin concentrations did not vary significantly with age between 8 and 18 months (table 1), although individual haemoglobin concentrations were observed to fluctuate over time. Haemoglobin concentrations at 8, 12, and 18 months of age were significantly higher in first born children. At 18 months girls had on average, borderline significantly higher concentrations of haemoglobin than boys (p = 0.051); children whose mothers' highest

Table 1 Descriptive statistics for haemoglobin concentrations in children at 8, 12, and 18 months of age and associations with confounding factors

	Haemoglobin concentrations (g/l)		
	8 mth	*12 mth*	*18 mth*
Overall			
Mean (SD)	117 (1.1)	118 (1.0)	117 (0.9)
N	942	835	810
Range	72–153	72–147	75–176
Confounders			
Parity			
0	118 (1.2)	119 (1.0)	118 (1.0)
1	116 (1.1)	116 (1.0)	116 (1.0)
2+	116 (1.1)	116 (1.0)	116 (0.9)
	0.006	<0.0001	0.006
Sex			
Male	117 (1.2)	117 (1.0)	116 (0.9)
Female	117 (1.1)	118 (1.0)	117 (0.9)
	0.619	0.486	0.051
Ethnicity			
White	117 (1.1)	118 (1.0)	117 (1.0)
Non-white	117 (1.4)	119 (0.6)	118 (0.8)
	0.9	0.7	0.7
Breast fed			
No	119 (1.0)	119 (1.1)	117 (0.9)
Yes	117 (1.2)	117 (1.0)	117 (1.0)
	0.020	0.2	0.9
Smoking			
No	117 (1.2)	117 (1.0)	117 (0.9)
Yes	118 (1.1)	118 (1.0)	117 (1.0)
	0.3	0.4	0.5
Maternal education			
A	117 (1.1)	119 (0.9)	117 (0.8)
B	118 (1.2)	116 (1.0)	116 (1.2)
C	117 (1.2)	116 (1.0)	116 (1.0)
D	118 (1.1)	118 (1.1)	117 (0.8)
E	116 (1.1)	119 (1.0)	119 (1.1)
	0.465	0.057	0.041

educational qualification was at least degree level (level E), had higher concentrations of haemoglobin compared to children whose mothers' highest educational qualification was A level (level D) or lower (p = 0.041). These effects of gender and maternal education were not found with haemoglobin concentrations at 8 or 12 months of age. Breast fed infants had significantly lower haemoglobin concentrations at 8 months of age than infants never breast fed in the first six months (p = 0.02), but this effect did not persist for haemoglobin concentrations measured at 12 and 18 months of age. Neither maternal smoking during pregnancy nor ethnicity was significantly associated with haemoglobin concentrations in children at 8, 12, or 18 months of age. The differences we have reported here, although statistically significant, were small and may not be clinically important. The power in this study to detect very small differences was high as a result of the size of the sample.

DEVELOPMENTAL OUTCOME

Table 2 presents mean (SD) overall scores for the five Griffiths subscales and development quotient (DQ). With the exception of scores on the hearing and speech subscale, average scores in the ALSPAC population were higher than the published norms. The Griffiths scales used were the "old" version, as the 1995 restandardisation was not available at the time of testing. Average scores on the hearing and speech, performance, social/personal, and DQ scales were significantly higher in children who were breast fed even for a short period in the first six months. First born children scored significantly higher in the hearing and speech and social/personal subscales and on the DQ. Scores on the locomotor and hand/eye subscales were not associated with maternal parity or breast feeding. As maternal educational achievement increased on a five point scale (level A–E), scores on all of the Griffiths

Table 2 Descriptive statistics for Griffiths scales of mental development at 18 months of age and associations with confounding factors

	Performance on Griffiths scales					
	Scale A (L)	*Scale B (HS)*	*Scale C (HE)*	*Scale D (P)*	*Scale E (S)*	*DQ*
Overall						
Mean (SD)	112 (10.1)	100 (16.1)	107 (10.3)	114 (12.7)	106 (10.9)	108 (8.8)
N	1141	1141	1141	1141	1141	1141
Range	64–136	63–133	64–134	64–136	64–131	65–130
Confounders						
Parity						
0	112 (9.8)	103 (16.6)	106 (10.2)	114 (13.0)	107 (10.5)	108 (8.9)
1	112 (9.8)	99 (15.3)	107 (9.9)	115 (11.9)	106 (10.9)	108 (8.5)
2+	112 (11.2)	95 (15.0)	106 (10.6)	112 (12.8)	104 (11.3)	106 (8.9)
	0.711	<0.0001	0.505	0.080	0.005	0.001
Sex						
Male	112 (10.2)	96 (15.3)	106 (10.1)	113 (13.2)	104 (10.8)	106 (8.6)
Female	112 (9.8)	104 (16.1)	107 (10.4)	115 (11.9)	108 (10.5)	109 (8.7)
	0.891	<0.0001	0.002	0.004	<0.0001	<0.0001
Ethnicity						
White	112 (10.1)	100 (16.2)	107 (10.3)	114 (12.8)	106 (10.9)	108 (8.8)
Non-white	113 (12.5)	98 (17.0)	106 (10.1)	114 (12.1)	107 (11.2)	108 (9.2)
	0.8	0.4	0.9	0.9	0.6	0.9
Breast fed						
No	111 (9.9)	97 (15.6)	106 (10.3)	111 (13.5)	103 (12.1)	106 (9.2)
Yes	112 (10.2)	101 (16.1)	107 (10.2)	114 (12.5)	107 (10.4)	108 (8.6)
	0.08	0.001	0.1	0.001	<0.0001	<0.0001
Smoking						
No	112 (10.2)	100 (16.2)	106 (10.4)	114 (12.6)	106 (10.8)	108 (8.9)
Yes	112 (10.0)	98 (15.5)	107 (9.0)	112 (12.5)	106 (10.9)	107 (8.0)
	0.8	0.1	0.9	0.03	0.6	0.2
Maternal education						
A	111 (11.3)	93 (14.0)	104 (10.4)	110 (13.9)	102 (12.8)	104 (9.1)
B	114 (10.2)	98 (15.9)	105 (9.6)	112 (12.3)	105 (10.7)	107 (8.1)
C	112 (9.7)	100 (15.9)	107 (10.1)	113 (12.5)	106 (10.4)	108 (8.5)
D	112 (10.1)	102 (16.3)	107 (10.3)	115 (12.7)	107 (10.6)	109 (9.0)
E	113 (10.3)	105 (16.4)	108 (10.3)	117 (11.6)	107 (9.7)	110 (8.5)
	0.5	<0.0001	<0.001	<0.0001	<0.0001	<0.0001

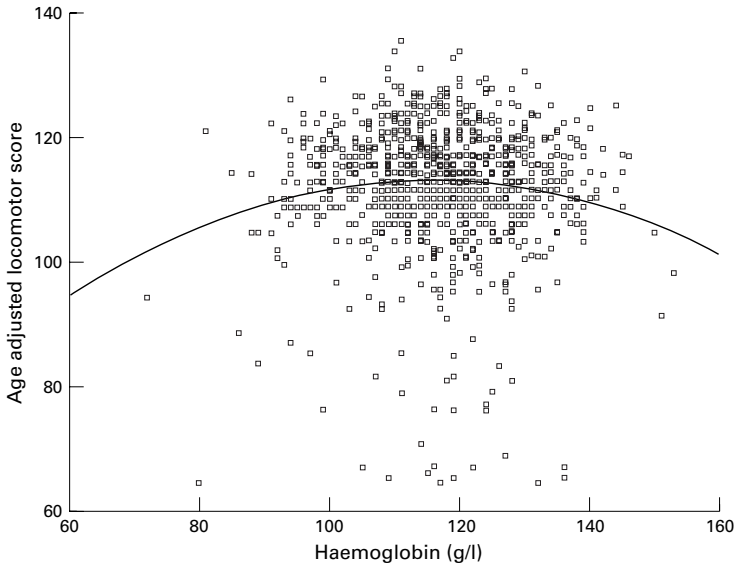

Figure 1 Regression curve of haemoglobin at 8 months and age adjusted locomotor score at 18 months.

subscales, with the exception of the locomotor scale, increased significantly. Children whose mothers smoked performed less well in the performance subscale than children of non-smoking mothers ($p = 0.031$), but smoking was not associated with impaired development in any other of the scales. Ethnicity was not statistically associated with performance in any of the Griffiths scales.

HAEMOGLOBIN AT 8 MONTHS AND DEVELOPMENTAL OUTCOME

Performance in the locomotor subscale at 18 months was highly significantly associated with haemoglobin concentrations at 8 months of age, and remained so after adjustment for maternal parity, sex of the child, breast feeding, maternal education, and Griffiths observer. A quadratic term for haemoglobin at 8 months was included in the model, reflecting the curvature of the data (adjusted p value for Hb = 0.001 and $Hb^2 = 0.002$). From the regression curve (fig 1) it was clear that scores on the locomotor subscale increased with increasing haemoglobin concentrations at 8 months and then plateaued. As haemoglobin concentrations further increased, scores on the locomotor subscale were observed to decrease. A similar trend was observed for performance in the hand/eye subscale, although statistical significance was borderline; after adjustment for confounding factors, the effect was no longer statistically significant (adjusted p value for Hb = 0.088; $Hb^2 = 0.086$). There may have been a quadratic association between haemoglobin at 8 months and performance on the DQ at 18 months, but after adjusting for possible confounders the effect was no longer statistically significant (adjusted p value for Hb = 0.102; $Hb^2 = 0.109$). There was no statistically significant association between haemoglobin concentrations at 8 months and performance in the remaining subscales.

Haemoglobin concentrations at 8 months were then categorised as described in the methods section in order to determine at which point(s) on the haemoglobin scale impaired development was evident. Table 3 presents the results of these analyses. Mean locomotor scores increased with increasing haemoglobin between 70 g/l and 95 g/l, after which they plateaued until haemoglobin exceeded 150 g/l and mean locomotor scores decreased (fig 1).

Table 3 Table of mean (SD) scores on Griffiths subscales that were associated with Hb concentrations at 8 or 12 months of age

	Griffiths subscales		
Hb concentration (g/l) at 8 mth (n)	*Locomotor scale A*	*Hand/eye scale B*	*DQ*
70–85 (4)	98 (25.4)	104 (11.2)	105 (12.3)
86–90 (6)	102 (12.8)	102 (4.6)	100 (7.6)
91–95 (24)	109 (9.6)	103 (9.8)	105 (7.4)
96–100 (44)	114 (9.2)	106 (10.4)	108 (8.2)
101–105 (56)	113 (9.3)	109 (10.8)	107 (9.0)
106–110 (108)	113 (9.6)	107 (9.6)	109 (8.3)
>110 (673)	112 (10.4)	106 (10.6)	107 (9.1)
⩾150 (3)	98 (6.7)	101 (6.1)	97 (6.4)
$p_{unadjusted}$	0.0013	0.422	0.05
$p_{adjusted}$	0.004	0.412	0.195

Differences between group means tested using ANOVA (p values given).

Excluding infants with Hb = 150 g/l (n = 3), infants with Hb < 95 g/l (n = 31) scored on average 6.6 points lower (>0.5 SD) on the locomotor subscale than infants with Hb ⩾ 95 g/l ($p = 0.001$), having adjusted for all other confounders. In the smaller group of children with Hb < 90 g/l (n = 10), average scores on the locomotor subscale were 12.5 points lower (>1 SD) than in infants with Hb ⩾ 90 g/l ($p = 0.0002$) after adjustment for all other confounders.

Table 3 also shows that there may have been a similar trend with performance on the hand/eye subscale and on the DQ when haemoglobin is categorised in the manner described above. However, mean differences between groups fail to reach statistical significance.

HAEMOGLOBIN AT 12 MONTHS AND DEVELOPMENTAL OUTCOME

There may have been a quadratic relation between haemoglobin concentrations in the children at 12 months of age and performance on the hearing and speech subscale of the Griffiths at 18 months. Statistical significance was borderline and remained so after adjustment for the confounding factors (adjusted p value for Hb = 0.068 and $Hb^2 = 0.086$). There were no children with Hb ⩾ 150 g/l at 12 months. Haemoglobin concentrations at 12 months of age were not statistically associated with performance on any of the remaining subscales, or the DQ.

HAEMOGLOBIN AT 18 MONTHS AND DEVELOPMENTAL OUTCOME

Haemoglobin concentrations measured on the day that the developmental tests were administered were not associated with performance on any of the subscales or the overall DQ.

Discussion

In this study we have shown that developmental outcome at 18 months of age, particularly

motor development, is associated with haemoglobin concentrations in children as young as 8 months. Haemoglobin concentrations below 96 g/l or haemoglobin concentrations of 150 g/l and above at 8 months were associated with lower scores in both the locomotor and hand/eye subscales and in the DQ of the Griffiths scales. This association was strongest by far for performance on the locomotor subscale. There is evidence that average scores on the locomotor subscale increase with increasing haemoglobin up to a point (Hb = 95 g/l) beyond which they plateau. There is no additional developmental benefit with increasing haemoglobin above 95 g/l. This effect was statistically strong and remained significant even after adjustment for a number of confounding factors. It also appeared that the highest band of haemoglobin at 8 months (≥150 g/l) was associated with impaired locomotor performance at 18 months, although the number of cases in this band was only three. All these three children were healthy, and none had evidence of any condition known to be associated with polycythaemia or delayed development. Excluding these three children from the analyses did not significantly alter the inferences from the models. In contrast, low haemoglobin concentrations at 12 and 18 months had a negligible effect on developmental outcome at 18 months.

The ALSPAC has a high response rate with participation from a diverse range of social backgrounds spanning urban, suburban, and rural communities with a low migration rate. The study sample is generally considered representative of the UK childhood population. Although certain social and ethnic groups are underrepresented in the Children in Focus cohort on whom this analysis is undertaken, our models include covariates for social background and ethnicity so that confounding should not have distorted our conclusions.

Not all children who had valid scores for the Griffiths scale administered at 18 months attended all three clinics or gave sufficient blood for haemoglobin assay at each clinic. However, further investigation revealed that these "non-responders" did not score significantly differently on any of the Griffiths scales compared to the "responders". The non-response also appeared random in terms of the main confounding factors: maternal education, breast feeding, gender, maternal smoking, and Griffiths tester. However, non-responders at 12 months were more likely to come from the non-white ethnic group (48.5% versus 27.4%) and to be first born (30.8% versus 25.8%). Given that the outcome measure is unaffected by non-response, it is highly unlikely that differences in ethnicity or maternal parity will have biased the results in any one direction.

Most other studies of the relation between anaemia and development have used the Bayley Scales,[18] although the fact that infants have been studied at different ages and with different levels of anaemia makes comparisons difficult. Studies have found between six and 12 point differences between anaemic and non-anaemic infants on both mental and motor scales using the Bayley. On the motor scales, items related to balance and independent walking were most affected, suggesting that anaemia is most damaging in the second half of the first year when these skills are being developed. We chose to use the Griffiths Scales[17] because they provide a larger number of subscales as well as a general development quotient (DQ). Our findings that the anaemic 8 month infants showed delay at 18 months in locomotor skills and to a lesser extent hand/eye coordination support the concept that a critical period of vulnerability to lack of iron, particularly in the development of motor skills, may occur some time before the age of 8 months.

As a result of the longitudinal nature of our study we were able to identify the age at which vulnerability to lack of iron appeared most damaging to infant development. We found that delayed development was primarily associated with anaemia at 8 months of age. Scores for the locomotor, hand/eye, and DQ were not associated with haemoglobin concentrations measured at 12 or 18 months of age. One possible explanation for this could be that children at the extremes of the haemoglobin distribution at 8 months might have been more likely to be lost to follow up at the 12 and 18 month clinics than children with normal haemoglobin concentrations, and so would not be represented in the 12 or 18 month analyses. However, this was not the case as this effect remained when we restricted the analysis to only those children who had blood assayed at all three time points (locomotor score associated with haemoglobin at 8 months: $p = 0.005$). Furthermore, we found that the majority of children with haemoglobin concentrations in the extremes of the distribution at 8 months of age appeared to have haemoglobin concentrations at 12 or 18 months within normal ranges, a phenomenon reported elsewhere.[19]

Our finding that mean scores on the locomotor and hand/eye subscales and general quotient were lower when Hb ⩾ 150 g/l is new, and suggests that a high as well as a low haemoglobin may delay development up to 18 months. Few British studies have been carried out on anaemia and developmental outcome using representative population based samples, and it is a result of the size of this study that we have sufficient power to find such an association. Even so, these data should be interpreted with caution as they are derived from only three individuals.

The question of the degree of anaemia necessary to cause developmental impairments is hampered by the problem that no satisfactory definition for infant anaemia has been established. Using the World Health Organisation's recommended guidelines on a cut off point for anaemia (Hb < 110 g/l), we found that at 8 months of age 23% of infants in our study would have been classified as anaemic.[19] We have previously suggested that a more representative cut off point for anaemia in 8 month old children would be 97 g/l, corresponding to the 5th centile of the distribution

of haemoglobin at this age. The discovery that motor and general development is delayed in children with haemoglobin concentrations at 8 months of age below 95 g/l reinforces the suggestion that this is a more realistic cut off. Previous studies using a cut off of 110 g/l may have used too wide a definition of anaemia and, by overestimating the number of anaemic cases, the effect of low haemoglobin on development may have been diluted.

In conclusion, this study provides supporting evidence for the concept of a vulnerable period in brain growth in the first 8 months of life, and suggests that the effects of anaemia may be most closely associated with motor development. At 18 months we found a clinically significant difference of more than one standard deviation in the locomotor scores of children with Hb $\leqslant$ 90 g/l at 8 months compared to the rest of the population. Impaired development was still observed in children with Hb $\leqslant$ 95 g/l compared with the rest of the population. There was no additional developmental advantage observed in children with Hb > 95 g/l, suggesting that a cut off of 110 g/l is not clinically appropriate for 8 month old infants. The results of this study suggest that, if screening is to be effective, it should be applied before 8 months of age, and interventions considered for infants with haemoglobin values at or below 95 g/l. We propose to investigate further the association between anaemia and development using more accurate and detailed long term outcomes as the children get older.

The Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) is part of the WHO initiated multicentre survey, the European Longitudinal Study of Pregnancy and Childhood (ELSPAC). The Children in Focus (CiF) substudy is, however, unique to ALSPAC. Specific funds for this anaemia study have been contributed by the South and West Regional Health Authority, the Department of Health, Cow and Gate, and the Meat and Livestock Commission. We gratefully acknowledge help in planning and conducting this anaemia study from Dr Petronella Clarke, Dr J James, Prof A Oakhill, Mr D Oakes, Mr N Farron, and Ms L McGrath. We are extremely grateful to all our funders, to the midwives, and other health professionals who made the survey possible, but most of all to the parents and children who have taken part. Further information about the ALSPAC study can be obtained from Professor Golding or from our website at http://www.ich.bris.ac.uk/alspac.html

1 Oski FA. Iron deficiency in infancy and childhood. *N Engl J Med* 1993;**329**:190–3.
2 Booth IW, Aukett A. Iron deficiency anaemia in infancy and early childhood. *Arch Dis Child* 1997;**67**:549–54.
3 Sherriff A, Emond AM, Hawkins N, Golding J, and the ALSPAC Children in Focus Study Team. Haemoglobin and ferritin concentrations in children aged 12 and 18 months. *Arch Dis Child* 1999;**80**:153–7.
4 Lozoff B, Jimenez E, Wolf AW. Long-term developmental outcome of infants with iron deficiency. *N Engl J Med* 1991;**325**:687–94.
5 Walter T, de Andraca I, Chadud P, Perales CG. Iron deficiency anemia: adverse effects on infant psycho-motor development. *Pediatrics* 1989;**84**:7–17.
6 de Andraca I, Castillo M, Walter T. Psychomotor development and behavior in iron-deficient anemic infants. *Nutr Rev* 1997;**55**:125–32.
7 Lansdown R, Wharton BA. Iron and mental and motor behaviour in children. In: *Iron. Nutrition and physiological significance*. Report of the British Nutrition Foundation Task Force. London: Chapman and Hall, 1995:65–8.
8 Aukett MA, Parks YA, Scott PH, Wharton BA. Treatment with iron increases weight gain and psychomotor development. *Arch Dis Child* 1986;**61**:849–57.
9 Idjradinata P, Pollitt E. Reversal of developmental delays in iron deficiency in infants treated with iron. *Lancet* 1993;**341**:1–4.
10 Lozoff B, Wolf AW, Jimenez E. Iron deficiency anemia and infant development: effects of extended iron therapy. *J Pediatr* 1996;**129**:382–9.
11 Williams J, Wolff A, Daly A, *et al*. Iron supplemented formulan milk related to reduction in psychomotor decline in infants from inner city areas: randomised study. *BMJ* 1999;**318**:693–7.
12 Yehuda S. Neurochemical basis of behavioural effects of brain iron deficiency in animals. In: Dobbing J, ed. *Brain behaviour and iron in the infant diet*. London: Springer-Verlag, 1990:63–81.
13 Kwik-Uribe CL, Golubt MS, Keen CL. Behavioral consequences of marginal iron deficiency during development in a murine model. *Neurotoxicol Teratol* 1999;**21**:661–72.
14 Grantham-McGregor S. A review of studies of the effect of severe malnutrition on mental development. *J Nutr* 1995;**125**(suppl 8):2233S–2238S.
15 Walter T, Kovalsky SJ, Stekel A. The effect of mild iron deficiency on infant developmental scores. *J Pediatr* 1983;**102**:519–22.
16 Emond AM, Hawkins N, Pennock C, Golding J, and the ALSPAC Children in Focus Team Haemoglobin and ferritin concentrations in infants at 8 months of age. *Arch Dis Child* 1996;**74**:228–39.
17 Griffiths R. *The abilities of young children: a comprehensive system of mental measurement for the first eight years of life*. Bucks, UK: The Test Agency, 1984.
18 Bayley N. *Bayley Scales of Infant Development*. New York: Psychological Corporation, 1969.
19 James JA, Laing GJ, Logan S, Rossdale M. Feasibility of screening toddlers for iron deficiency anaemia in general practice. *BMJ* 1997;**315**:102–3.