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Effect of iron supplementation during pregnancy on the behaviour of children at early school age: long-term follow-up of a randomised controlled trial

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Although routine Fe supplementation in pregnancy is a common practice, its clinical benefits or risks are uncertain. Children born to mothers in the Fe group in a trial of Fe supplementation in pregnancy have been found to have a significantly higher risk of abnormal behaviour at 4 years of age than those born to mothers in the placebo group. The objective of the present study therefore was to determine whether Fe supplementation in pregnancy influences child behaviour at early school age. The study was a follow-up of children at 6–8 years of age after women (*n* 430) were randomly allocated to receive a daily Fe supplement (20 mg) or placebo from 20 weeks gestation until delivery. The supplement reduced the incidence of Fe-deficiency anaemia at delivery from 9 % to 1 %. Child behaviour and temperament were assessed using the Strengths and Difficulties Questionnaire and the Short Temperament Scale for Children. Of the children, 264 (61 %) participated in the follow-up. Mean behaviour and temperament scores and the proportion of parent-rated and teacher-rated abnormal total difficulties scores did not differ between the Fe and placebo groups. However, the incidence of children with an abnormal teacher-rated peer problems subscale score was higher in the Fe group (eleven of 112 subjects; 8 %) than in the placebo group (three of 113 subjects; 2 %); the relative risk was 3·70 (95 % CI 1·06, 12·91; $P = 0·026$). We conclude that prenatal Fe supplementation had no consistent effect on child behaviour at early school age in this study population. Further investigation regarding the long-term effects of this common practice is warranted.

Iron supplementation: Pregnancy: Child behaviour: Industrialised countries

Routine Fe supplementation in pregnancy is a common practice to prevent Fe deficiency and Fe-deficiency anaemia, although expert opinion on this practice is divided. While pregnant women in the USA[1] are routinely advised to take Fe supplements of 30–60 mg/d, the policy in Australia[2] and the UK[3] is to screen pregnant women for anaemia and only treat those with Fe-deficiency anaemia. A reason for this is that although Fe supplementation in pregnancy improves maternal Fe status, there is a paucity of evidence of a clear clinical benefit for mothers[4,5]. The long-term effects of routine Fe supplementation on child development is also unclear[4,5]. We recently published a 4-year follow-up of the Adelaide Mothers' and Babies' Iron Trial (AMBIT), the first human intervention trial designed specifically to assess the effect of routine low-dose Fe supplementation (20 mg/d) on childhood intelligence quotient (IQ) and behaviour[6]. Our findings indicated that routine Fe supplementation in pregnancy had no effect on IQ at 4 years. There was, however, a higher incidence of abnormal behaviour reported by parents of children in the Fe group than in the placebo group[6]. Although this may have been a chance finding, the possibility that it reflects a true adverse effect of routine Fe supplementation in pregnancy in well-nourished populations cannot be overlooked. Animal studies have highlighted that both inadequate Fe nutrition in pregnancy and prenatal Fe overload are associated with persistent behavioural changes in offspring[7–9] regardless of later Fe status or later Fe supplementation[7]. The aim of the present study was to assess whether routine Fe supplementation in pregnancy in a well-nourished population affects child behaviour at early school age through further follow-up of the children born in the AMBIT.

Subjects and methods

Participants

Participants were children born in the AMBIT, a double-blind randomised controlled trial of Fe supplementation in pregnancy[10]. The original trial was conducted between 1997 and 1999. Four hundred and thirty non-anaemic pregnant

Abbreviations: AMBIT, Adelaide Mothers' and Babies' Iron Trial; IQ, intelligence quotient; SDQ, Strengths and Difficulties Questionnaire; STSC, Short Temperament Scale for Children.

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women receiving antenatal care at the Children, Youth and Women's Health Services in Adelaide, Australia were recruited to participate. Women were randomly allocated to receive either low-dose Fe (20 mg/d) or placebo from 20 weeks gestation until delivery. The low-dose supplement was designed to increase Fe intake to the recommended dietary intake for pregnant women in Australia at that time, 22–36 mg/d[11]. The compliance rate was 86 % for both groups and the dietary intake of Fe during pregnancy also did not differ between groups (13·0 (SD 5·4) mg/d in the Fe group and 13·6 (SD 5·4) mg/d in the control group; $P=0·299$)[10]. The incidence of Fe-deficiency anaemia and Fe deficiency in women at delivery was significantly lower in the Fe group than in the placebo group (Table 1). The present follow-up was conducted between April and November 2006 when the children born in the AMBIT were between 6 and 8 years old. Participation in the 4-year follow-up[6] was not a prerequisite for participation in this school-age follow-up and an attempt was made to contact all mothers and children enrolled in the original study. In the present paper children are referred to as belonging to the Fe or the placebo group according to their mother's group allocation in the AMBIT. The present study was approved by the Children, Youth and Women's Health Services Research Ethics Committee. Informed consent was obtained from the families of all participants.

Assessments

The primary outcome was child behaviour assessed using parent-rated and teacher-rated versions of the Strengths and Difficulties Questionnaire (SDQ)[12] for 4–10-year-olds. The SDQ is an internationally validated brief screening measure used to assess behavioural problems[13]. It was chosen as the primary outcome because it was used to assess behaviour in the 4-year AMBIT follow-up in which a higher incidence of total difficult behaviours was reported by parents in the Fe group compared with control[6]. The SDQ has five subscales (conduct problems, peer problems, hyperactivity, emotional symptoms and prosocial behaviour)

Table 1. The demographic characteristics of participating families

	Mother's group assignment in AMBIT				
	Fe (*n* 132)		Placebo (*n* 132)		
	n	%	*n*	%	*P*
Maternal characteristics					
Age at enrolment in AMBIT (years)					0·731
Mean	29·3		29·5		
SD	4·8		4·7		
Education level					0·925
≤ 12 years	92	70	92	70	
Diploma or degree	40	30	39	30	
Occupation score*					0·232
Mean	4·9		4·8		
SD	0·8		0·9		
Smoked in pregnancy	22	17	19	14	0·610
Fe status at birth (*n*/*N*)					
ID	36/122	30	64/119	54	<0·001
IDA	1/124	1	11/125	9	0·003
Characteristics of children					
Age (years)					0·277
Mean	7·5		7·6		
SD	0·4		0·4		
Male sex	74	56	62	47	0·139
Birth order					0·967
1	63	48	65	49	
2	49	37	48	36	
≥ 3	20	15	19	14	
Gestational age at birth (weeks)					0·208
Mean	39·6		39·3		
SD	1·9		2·0		
Breastfed ≥ 6 months	57	44	58	45	0·857
Recent life events					
Number of events in the last year					0·120
Mean	2·1		2·6		
SD	2·2		2·5		
Number of events having an effect					0·454
Mean	0·9		1·0		
SD	1·4		1·7		
General family functioning score					0·053
Mean	1·5		1·6		
SD	0·5		0·5		

AMBIT, Adelaide Mothers' and Babies' Iron Trial; ID, Fe deficiency (defined as ferritin < 12 μg/l); IDA, Fe-deficiency anaemia (defined as Hb < 110 g/l and ferritin < 12 μg/l).
* Ranked according to the scale by Daniel[25]. The higher the score, the lower the skilled occupation.

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in addition to a combined total difficulties scale. Total difficulties scores and subscale scores are defined as 'normal' and 'abnormal' according to SDQ cut-offs[14]. The questionnaire has moderate-to-strong internal reliability, test–retest reliability and external validity[13,15]. In addition to the SDQ, parents were also asked whether they had ever consulted a healthcare professional about difficulties with their child's behaviour and, if they had, to provide details of the consultation.

The secondary outcome was child temperament assessed using the parent-rated Short Temperament Scale for Children (STSC)[16]. This was included to support the SDQ because temperament reflects behavioural style. Children with a history of behavioural problems have more consistently difficult temperaments than their counterparts without behavioural problems[16]. The STSC has four subscales (approach, persistence, rhythmicity and inflexibility) in addition to a total easy–difficult temperament scale. The STSC has strong internal consistency and was developed after factor analysis of the longer Childhood Temperament Questionnaire[17]. A total easy–difficult temperament score of $>$ 1 SD above the population mean is indicative of a difficult temperament[16].

To assess the effect of potential covariates, parents were also asked to complete two brief measures of risk factors for behavioural problems in children. A Recent Life Events questionnaire[18] was used to assess the number and impact of life events in the family, while the General Functioning Subscale of the McMaster Family Assessment Device[19] was used to assess the healthiness of the family unit. Information regarding sex, gestational age at birth, birth order, duration of breast-feeding, maternal smoking in pregnancy, parental education and occupation were extracted from the original AMBIT dataset[10].

Research staff involved in data collection were blinded to the group assignment until all primary analyses were completed. Mothers had the opportunity to learn their group allocation in the AMBIT at the conclusion of the 4-year follow-up[6] but were not reinformed during the present follow-up.

Statistical analysis

The data were analysed using SPSS software (version 10.0.1; SPSS Inc., Chicago, IL, USA). The primary analyses were based on intention to treat. Mean scores for parent-rated child behaviour, child temperament and teacher-rated child behaviour were compared between the Fe and placebo groups using independent samples *t* tests. Differences between categorical variables such as SDQ scores dichotomised to 'normal' and 'abnormal' were compared using χ^2 tests. Statistical significance was set at a *P* value $<0{\cdot}05$ for all statistical tests. Regression analyses were conducted to examine the influence of potential covariates on group comparisons. Selection of potential covariates was based on independent predictors cited in the literature as influencing child behaviour and those maternal and child characteristics where the *P* value for comparison between groups was 0·2 or less.

Results

Characteristics of the participants

A total of 61 % (264 out of 433 subjects) of the children born in the AMBIT were assessed at follow-up (Fig. 1). A total of 89 % (236 out of 264 subjects) of the children who participated

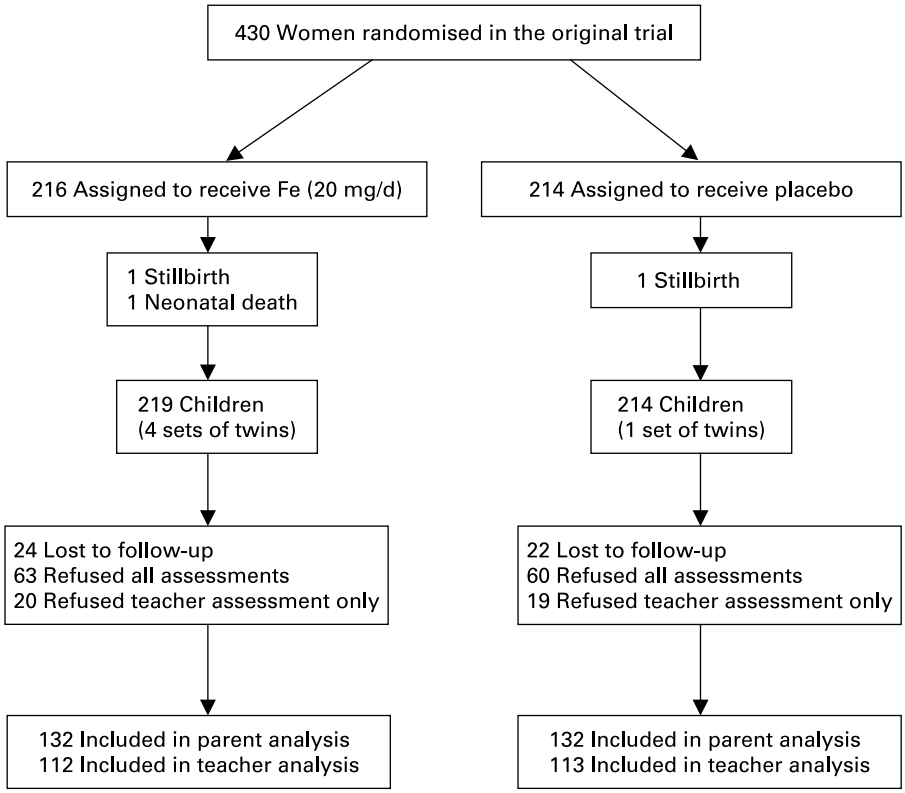

Fig. 1. Flow diagram of the original Fe trial and the early school-age follow-up.

in this follow-up also participated in the 4-year follow-up. All children had at least 1 year of schooling at the time of assessment because children start school at age 5 years in Adelaide where the study was conducted. The social and demographic characteristics of participating families did not differ between the Fe and placebo groups (Table 1). The difference in maternal Fe status at the conclusion of the original trial (at birth) between the Fe and placebo groups remained significant among follow-up participants. There were significant differences between the socio-demographic characteristics of participants and non-participants. Mothers of children who did not participate were generally younger than participating mothers ($P=0{\cdot}016$). They were also more likely to have a lower skilled occupation and to have smoked during pregnancy, and less likely to have breastfed their child, than the mothers of participating children ($P<0{\cdot}05$ for all).

Child behaviour

The mean scores for parent-rated and teacher-rated SDQ scores did not differ between the Fe and placebo groups (Table 2). There was no difference in the proportion of children with abnormal parent-rated behaviour scores in the two groups (Table 3). There was a higher incidence of abnormal teacher-rated peer problems scores in the Fe group than the placebo group (Table 3). The relative risk was 3·70 (Table 3). Adjustment for potential covariates including family functioning and sex of the child did not affect the statistical significance of any analyses for the behaviour outcome. There were strong positive correlations between parent-rated and teacher-rated total difficulties scores (r 0·587; $P<0{\cdot}001$) as well as parent-rated total difficulties scores between the 4-year follow-up[6] and the present follow-up (r 0·593; $P<0{\cdot}001$). Among the thirty-six children who had an abnormal parent-rated total difficulties score at the 4-year follow-up[6], twenty-five of them participated in the present study and ten of the twenty-five remained abnormal. There was no significant association between a behavioural consultation and group allocation (twenty-seven of 132 (20 %) children in the Fe group compared with twenty-one of 132 (16 %) children in the placebo group; $P=0{\cdot}353$). There were significant differences between the behaviour and temperament scores of those children who had a behavioural consultation and those who had not. Children who had had a consultation for their behaviour had higher parent-rated total difficulties scores than those who had not (16·0 (SD 5·9) compared with 7·3 (SD 4·9) for the parent-rated SDQ; mean difference 8·74 (95 % CI 7, 11); $P<0{\cdot}001$); they also had higher teacher-rated total difficulties scores than those who had not had a consultation (13·0 (SD 7·9) compared with 5·3 (SD 7·4) for the teacher-rated SDQ; mean difference 10·25 (95 % CI 5, 10); $P<0{\cdot}001$).

Child temperament

There was no difference between either mean temperament scores or the proportion of children with difficult temperament scores in the Fe and placebo groups (Tables 4 and 5). There was a strong correlation between parent-rated behaviour total difficulties scores and total temperament scores (r 0·637; $P<0{\cdot}001$). Children who had consulted a health professional for behavioural problems had more difficult temperament ratings than those who had not (3·5 (SD 0·6) compared with 2·8 (SD 0·5); mean difference 0·74 (95 % CI 0·6, 0·9); $P<0{\cdot}001$).

Discussion

This is the first human intervention trial to assess the long-term effects of routine Fe supplementation in pregnancy on child behaviour and development. The present results demonstrate that Fe supplementation in pregnancy had no clear beneficial or adverse effect on parental reports of child behaviour and temperament when the children were 6–8 years of age. There was also no difference in the incidence of teacher-rated total abnormal behaviour scores in the two groups. However, significantly

Table 2. Parent-rated and teacher-rated behaviour scores
(Mean values and standard deviations)

	Mother's group assignment in AMBIT						
	Fe		Placebo				
	Mean	SD	Mean	SD	MD	95 % CI	*P*
Parent-rated SDQ (*n*)	132		132				
Emotion	2·0	2·1[2]	2·3	2·1	−0·32	−0·83,0·18	0·212
Conduct	1·7	1·8	1·9	1·9	−0·23	−0·67,0·21	0·301
Hyperactivity	3·6	2·9	3·6	2·6	−0·05	−0·73,0·63	0·883
Peer problems	1·4	1·6	1·4	1·6	−0·02	−0·40,0·37	0·939
Prosocial behaviour	8·1	1·8	8·0	1·9	−0·06	−0·38,0·50	0·787
Total difficulties score	8·6	6·3	9·2	5·9	−0·62	−2·10,0·87	0·412
Teacher-rated SDQ (*n*)	112		113				
Emotion	1·4	1·8	1·7	2·2	−0·31	−0·83,0·21	0·239
Conduct	1·0	1·9	0·9	1·5	−0·07	−0·37,0·52	0·755
Hyperactivity	2·9	2·9	3·0	3·2	−0·17	−0·97,0·64	0·683
Peer problems	1·4	1·9	1·2	1·4	−0·25	−0·18,0·69	0·256
Prosocial behaviour	7·9	2·2	7·7	2·3	−0·15	−0·44,0·74	0·615
Total difficulties score	6·7	6·2	6·8	6·3	−0·16	−1·80,1·48	0·851

AMBIT, Adelaide Mothers' and Babies' Iron Trial; MD, mean difference; SDQ, Strengths and Difficulties Questionnaire.

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Table 3. Proportion of children with abnormal behaviour ratings on the Strengths and Difficulties Questionnaire (SDQ)

	Mother's group assignment in AMBIT						
	Fe		Placebo				
	n	%	*n*	%	RR	95% CI	*P*
Abnormal parent-rated SDQ (*n*)	132		132				
Emotion (score ≧ 5)	18	14	16	12	1·13	0·60, 2·11	0·713
Conduct (≥ 4)	20	15	23	17	0·87	0·50, 1·51	0·617
Hyperactivity (≥ 7)	23	17	22	17	1·05	0·61, 1·78	0·870
Peer problems (≥ 4)	16	12	13	10	1·23	0·62, 2·46	0·555
Prosocial behaviour (≤ 4)	7	5	6	5	1·12	0·40, 3·38	0·776
Total difficulties score (≥ 17)	15	11	17	13	0·88	0·46, 1·69	0·706
Abnormal teacher-rated SDQ (*n*)	112		113				
Emotion (score ≥ 6)	4	3	9	7	0·45	0·14, 1·41	0·158
Conduct (≥ 4)	9	7	8	6	1·14	0·45, 2·84	0·786
Hyperactivity (≥ 7)	12	9	22	17	0·55	0·29, 1·06	0·067
Peer problems (≥ 5)	11	8	3	2	3·70	1·06, 12·91	0·026
Prosocial behaviour (≤ 4)	9	7	14	11	0·65	0·29, 1·44	0·281
Total difficulties score (≥ 16)	10	8	13	10	0·78	0·36, 1·70	0·524

AMBIT, Adelaide Mothers' and Babies' Iron Trial; RR, relative risk.

more children in the Fe group had an abnormal teacher-rated peer problems score than in the placebo group.

Although the majority of data collected in the present study from multiple assessments indicate no effect of Fe supplementation in pregnancy of childhood behaviour at early school age, our single report of a higher incidence of abnormal peer problems rated by teachers in the Fe group deserves some attention because the effect is consistent with our earlier observations when the children were 4 years of age[6]. The only other human study to suggest that a high Fe supply to the fetus may adversely affect early childhood development was a cohort study involving largely small-for-gestational-age infants[20]. They reported that children with cord serum ferritin levels in the highest quartile scored lower on developmental tests including Full Scale IQ than children with cord serum ferritin levels in the two middle quartiles. Children with cord ferritin in the lowest quartile also scored lower than the median quartiles on some measures. While the investigators suggested that ferritin levels in the highest quartile may have been falsely elevated due to maternal infection, it is plausible that the high cord ferritin levels (high Fe status) adversely affected child development. These data are supported by an animal study that showed excessive Fe exposure during the neonatal period altered long-term neurobehavioural outcome, including motor behaviour and radial arm maze learning[9].

On the other hand, the incidence of abnormal teacher-rated peer problems was relatively small and it is not possible to exclude that this is a chance effect because of limited sample size. The difference in teacher-rated abnormal peer problems scores was not reflected in the corresponding peer problems subscale in the parent-rated SDQ. The number of teacher questionnaires returned was less than the number of parent questionnaires and it is possible that an increased teacher response rate might have reduced the variance in scores to the level of the parent-rated scores. Conversely, it is likely that teachers witness a range of peer interactions that parents are not privy to, and this may be why the ratings vary between the two versions of the SDQ. When multiple informants are used, clinician and researcher assessments can differ depending on the information sources used in assessment and the weight given to information from different sources where disagreement exists[21]. However, Goodman[13] reported better inter-rater correlations between the parent and teacher versions of the SDQ than for other behavioural measures such as the Child Behaviour Checklist.

The parent-rated SDQ and STSC scores of the children reflect normative data for the Australian population[15,17]. The parent-rated SDQ total difficulties score and the STSC easy–difficult temperament score correlated well, reflecting consistency in parent answers and increasing confidence in the ability of

Table 4. Child temperament: parent-rated temperament score (Mean values and standard deviations)

	Mother's group assignment in AMBIT						
	Fe (*n* 132)		Placebo (*n* 132)				
	Mean	SD	Mean	SD	MD	95% CI	*P*
Approach	2·8	1·0	2·9	1·0	−0·04	−0·29, 0·20	0·725
Rhythmicity	2·5	0·8	2·6	0·8	−0·02	−0·22, 0·18	0·855
Inflexibility	2·7	1·0	2·8	1·0	−0·07	−0·31, 0·17	0·584
Persistence	3·1	0·9	3·0	0·8	−0·06	−0·14, 0·27	0·563
Total easy–difficult temperament	2·9	0·7	2·9	0·5	−0·02	−0·17, 0·14	0·827

AMBIT, Adelaide Mothers' and Babies' Iron Trial; MD, mean difference.

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Table 5. Child temperament: difficult temperament*

	Mother's group assignment in AMBIT						
	Fe (*n* 132)		Placebo (*n* 132)				
	n	%	*n*	%	RR	95 % CI	*P*
Approach	21	16	19	14	1·11	0·62, 1·96	0·731
Rhythmicity	23	17	24	18	0·96	0·57, 1·61	0·872
Inflexibility	24	18	19	14	1·26	0·73, 2·19	0·405
Persistence	29	22	19	14	1·53	0·90, 2·58	0·111
Total easy–difficult temperament	23	17	20	15	1·15	0·66, 1·99	0·617

AMBIT, Adelaide Mothers' and Babies' Iron Trial; RR, relative risk.
* Defined as a score 1 SD above the sample mean[16].

these measures to identify common themes in both behaviour and temperament. Adjustment for the difference in potential confounding factors of behaviour between groups including family functioning did not alter the study findings.

A potential limitation of the present study was a relatively high attrition rate although it is better or comparable with that of other long-term follow-up studies of perinatal nutrition interventions[22,23]. There were also significant differences between the socio-demographic characteristics of participants and non-participants. Similar differences have also been documented in other long-term nutritional studies[24]. Women with a young maternal age, low education level, who smoke during pregnancy or do not breastfeed their child are less likely to comply with the study treatment and more likely to withdraw or be lost to follow-up[24]. Despite these factors, the present study had high internal validity. Participation rates were equal across the two groups, there were no differences in the baseline characteristics of the groups and the effect of the intervention (the incidence of Fe deficiency and Fe-deficiency anaemia at delivery) remained significant and equivalent in size to that seen in the original report[10]. These points highlight the overall strength of the present report as a long-term follow-up of a randomised controlled trial designed to investigate causal relationships.

In summary, our data suggest that routine Fe supplementation in pregnancy in an otherwise well-nourished population has no effect on behaviour and may even have a negative influence. However, our findings may not generalise to other populations where Fe deficiency in pregnancy is more severe. Our earlier follow-up of the same children showed no effect on IQ[6], and other randomised controlled trials of prophylactic Fe supplementation in pregnancy suggest that Fe does not improve pregnancy outcomes[4,5]. Taken together, these data indicate that routine Fe supplementation of well-nourished women in pregnancy has no detectable benefit in terms of clinical measures beyond improved maternal Fe status and raise the possibility of an adverse outcome on child behaviour. It is therefore prudent that this widespread practice be re-evaluated in industrialised countries.

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References

1. Centers for Disease Control and Prevention (1998) Recommendations to prevent and control iron deficiency in the United States. *MMWR* **47**, 1–29.
2. Australian Iron Status Advisory Panel (2001) Iron Status and Pregnancy: Current Practice. Recommended Guidelines. http://www.ironpanel.org.au/AIS/AISdocs/pregdocs/preg36.html (accessed July 2007).
3. National Collaborating Centre for Women's and Children's Health (2003) *Routine Care for the Healthy Pregnant Women: Clinical Guideline*, p. 9. London: National Institute for Clinical Excellence.
4. US Preventive Services Task Force (1993) Routine iron supplementation during pregnancy. *JAMA* **270**, 2848–2854.
5. Mahomed K (2003) Iron supplementation in pregnancy. *The Cochrane Database of Systematic Reviews 2003,* issue 2, CD000117. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000117/frame.html
6. Zhou SJ, Gibson RA, Crowther CA, Baghurst PAH & Makrides M (2006) Effect of iron supplementation in pregnancy on IQ and behavior of children at 4 years: long term follow up of a randomized controlled trial. *Am J Clin Nutr* **83**, 1112–1117.
7. Kwik-Uribe CL, Golub MS & Keen CL (2000) Chronic marginal iron intakes during early development in mice alter brain iron concentrations and behavior despite postnatal iron supplementation. *J Nutr* **130**, 2040–2048.
8. deUngria M, Rao R, Wobken JD, Luciana M, Nelson CA & Georgieff MK (2000) Perinatal iron deficiency decreases cytochrome c oxidase (CytOx) activity in selected regions of neonatal rat brain. *Pediatr Res* **48**, 169–176.
9. Fredriksson A, Schroder N, Eriksson P, Izquierdo I & Archer T (1999) Neonatal iron exposure induces neurobehavioral dysfunctions in adult mice. *Toxicol Appl Pharmacol* **159**, 25–30.

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10. Makrides M, Crowther CA, Gibson RA, Gibson RS & Skeaff CM (2003) Efficacy and tolerability of low-dose iron supplements during pregnancy: a randomized controlled trial. *Am J Clin Nutr* **78**, 145–153.
11. National Health and Medical Research Council (1991) *Recommended Dietary Intakes for Use in Australia*. Canberra: Australian Government Publishing Service.
12. Goodman R (2006) Strengths and Difficulties Questionnaire version February 2006. http://sdqinfo.com/ba3.html (accessed February 2006).
13. Goodman R (2001) Psychometric properties of the Strengths and Difficulties Questionnaire. *J Am Acad Child Adolesc Psychiatry* **40**, 1337–1345.
14. Goodman R (2006) Scoring the Informant-Rated Strengths and Difficulties Questionnaire, version February 2006. http://www.sdqinfo.com/ScoreSheets/el.pdf (accessed February 2006).
15. Hawes DJ & Dadds MR (2004) Australian data and psychometric properties of the Strengths and Difficulties Questionnaire. *Aust N Z J Psychiatry* **38**, 644–651.
16. Prior M, Sanson A, Smart D & Oberklaid F (2000) *Pathways from Infancy to Adolescence: Australian Temperament Project 1983–2000*. Melbourne: Australian Institute of Family Studies.
17. Sanson A, Smart D, Prior M, Oberklaid F & Pedlow R (1994) The structure of temperament from three to seven years: age, sex and sociodemographic differences. *Merrill-Palmer Q* **40**, 233–252.
18. Department of Health, Cox A & Bentovim A (2000) *The Family Pack of Questionnaires and Scales*. London: The Stationery Office.
19. Epstein NB, Baldwin LM & Bishop DS (1983) The McMaster family assessment device. *J Marital Fam Ther* **9**, 171–180.
20. Tamura T, Goldenberg RL, Hou J, Johnston KE, Cliver SP, Ramey SL & Nelson KG (2002) Cord serum ferritin concentrations and mental and psychomotor development of children at five years of age. *J Pediatr* **140**, 165–170.
21. Sawyer MG, Baghurst P & Clark J (1992) Differences between reports from children, parents and teachers: implications for epidemiological studies. *Aust N Z J Psychiatry* **26**, 652–660.
22. Helland IB, Smith L, Saarem K, Saugstad OD & Drevon CA (2003) Maternal supplementation with very-long-chain *n*-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. *Pediatrics* **111**, e39–e44.
23. Tamura T, Goldenberg RL, Ramey SL, Nelson KG & Chapman VR (2003) Effect of zinc supplementation of pregnant women on the mental and psychomotor development of their children at 5 y of age. *Am J Clin Nutr* **77**, 1512–1516.
24. Schoetzau A, Gehring U, Franke K, Grubl A, Koletzko S, von Berg A, Berdel D, Reinhardt D, Bauer CP & Wichmann H-E (2002) Maternal compliance with nutritional recommendations in an allergy preventive programme. *Arch Dis Child* **86**, 180–184.
25. Daniel A (1983) *Power, Privilege and Prestige: Occupations in Australia*, 1st ed. Melbourne: Longman-Cheshire.

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