Absorption of non-haem iron from food during normal pregnancy

Jon F R Barrett, Paul G Whittaker, John G Williams, Tom Lind

Abstract

***Objective*—To determine whether the increased iron demands of pregnancy could be met by increased absorption from dietary sources.**

***Design and setting*—Longitudinal prospective study in the research unit of a maternity hospital.**

***Subjects*—12 normal pregnant women.**

***Interventions*—At 12, 24, and 36 weeks' gestation (within one week) and 16-24 weeks after delivery women ate a breakfast of meat, bread, and orange juice (3·2 mg iron), extrinsically labelled with the stable isotope iron-54 (2·8 mg); the stable isotope iron-57 (200 μg) was given intravenously.**

***Main outcome measures*—Serum samples were taken for 10 hours after administration of the isotopes; ratios of the isotopes were measured by inductively coupled plasma mass spectrometry, and the absorption of oral iron was calculated.**

***Results*—The geometric mean (95% confidence interval) absorption of iron at 12, 24, and 36 weeks' gestation was 7% (5% to 11%), 36% (28% to 47%), and 66% (57% to 76%) respectively. At 16-24 weeks after delivery the absorption was 11% (6% to 21%). The mean increase in absorption at 36 weeks (compared with that at 12 weeks) was 9·1 times (6·0 to 13·7). One pregnant woman developed iron deficiency anaemia but was otherwise indistinguishable from the others.**

***Conclusions*—An increase in the absorption of iron from food is a physiological consequence of normal pregnancy, not the result of developing anaemia during pregnancy, and such an increase is large enough to meet the increased requirements of pregnancy provided that the dietary intake is adequate.**

University Department of Obstetrics and Gynaecology, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP
Jon F R Barrett, *research registrar*
Paul G Whittaker, *lecturer in clinical science*
Tom Lind, *professor of reproductive physiology*

Natural Environmental Research Council ICP-MS Facility, Imperial College at Silwood Park, Ascot, Berkshire SL5 7TE
John G Williams, *research manager*

Correspondence to:
Dr Whittaker.

BMJ 1994;309:79-82

Introduction

The need for routine iron supplements during pregnancy remains a longstanding controversy in obstetrics.[1,2] Changes in haematological variables may result from normal maternal physiological adaptations rather than represent true iron deficiency anaemia.[3,4] Haemoglobin, serum iron, and ferritin concentrations are reduced in early pregnancy both in women who are taking supplements and in women who are not, and they increase again by the sixth day after delivery.[5] This suggests that during pregnancy other factors, possibly humoral, disturb the relation that usually exists between serum ferritin concentration and iron stores. Although the haemoglobin concentrations in women who are given iron supplements return to prepregnancy values in the third trimester, the supplements may cause macrocytosis.[3] Definitions of haematological normality and anaemia during pregnancy have usually been derived from women who are not pregnant or who are already taking iron tablets.[6,7]

Studies with radioisotopes and stable isotopes have shown that aqueous iron absorption increases during pregnancy[8-10] but have not answered the question of whether the increased iron demands of a singleton pregnancy can be met by increased absorption from the daily diet. We aimed to provide an answer with a serial study of absorption of non-haem iron from food during pregnancy.

Materials and methods

PREPARATION OF ISOTOPES

Iron isotopes were obtained as wire from Techsnabexport, London, England. Their abundances for enriched iron-54 were ^{54}Fe 99·85%, ^{56}Fe 0·13%, ^{57}Fe 0·02%, and ^{58}Fe 0% and for enriched iron-57 were ^{54}Fe 0%, ^{56}Fe 0·57%, ^{57}Fe 95·93%, and ^{58}Fe 3·5%. The natural abundances of elemental iron isotopes are ^{54}Fe 5·8%, ^{56}Fe 91·72%, ^{57}Fe 2·2%, and ^{58}Fe 0·28%.[11]

Iron-54 for oral use was mixed with 0·5M sulphuric acid (10 mg to 1 ml) and heated to 50° C until dissolved. Ascorbic acid (at a final concentration of 3 mg/ml) and deaerated, deionised water were added, which gave a final iron concentration of 2·83 mg per 5 ml. The solutions were sterilised by filtration into ampoules and sealed under nitrogen. Iron-57 for intravenous use was made up similarly except that 10 mg of iron was mixed with 3 ml of 0·5M sulphuric acid, which resulted in a final iron concentration of 200 μg per 2 ml. The final pH of the intravenous solution was 1·7 to ensure stability during storage but was diluted in saline immediately before injection.

SUBJECTS

Twelve women who were pregnant for the first time were recruited from the antenatal clinic at the Royal Victoria Infirmary, Newcastle upon Tyne, at 8-10 weeks' gestation; this sample size was calculated from previous work to be sufficient to show the effects of pregnancy on the absorption of iron.

We selected healthy women with no history of serious illness who had not taken iron supplements, were non-smokers, and in whom laboratory tests had shown no anaemia or iron deficiency (see below). Each woman was studied three times during pregnancy, at 12, 24, and 36 weeks' gestation (within one week), and once 16-24 (average 18) weeks after delivery provided that normal menstruation had resumed and lactation had stopped. Four of the women were not studied after delivery: two had received oral iron supplements to correct anaemia resulting from a postpartum haemorrhage; one was still breast feeding at the end of the project and had not resumed normal menstruation; and with one technical problems occurred with the isotope infusion and the subject declined to be studied on a further occasion.

All women gave informed consent, and the project was approved by the ethics committee of Newcastle Regional Health Authority.

ADMINISTRATION OF ISOTOPES AND LABELLING OF FOOD

For three days before the study each subject fol-

lowed a diet plan that provided a daily dietary intake of 13 mg of iron (an average of 4 mg from meat), with the iron content of the food determined from tables.[12] The subjects attended the research unit in the morning having fasted overnight. An intravenous cannula was inserted into each arm of each subject and flushed with heparinised saline to prevent clotting. A 20 ml blood sample was taken for the measurement of basal isotope ratios, full blood count, and serum ferritin and red cell zinc protoporphyrin concentrations. Haematological variables were determined on the same day with a Coulter counter (Coulter Electronics, Luton, England). The coefficient of variation of 17 duplicate samples was 0·9% for haemoglobin and 0·7% for mean cell volume. Serum ferritin concentration was measured by radioimmunoassay (Becton Dickinson, Cowley, England; coefficient of variation 5·2%) and zinc protoporphyrin with a haematofluorometer (AVIV Biomedical, Lakewood, New Jersey, United States; coefficient of variation 1·2%).

The cannula in the left arm was connected to a 500 ml bag of warmed normal saline and allowed to infuse slowly. An ampoule (200 μg) of iron-57 was taken up into a syringe with 10 ml of saline and was given intravenously into the left arm. The syringe was flushed clean from the infusing rider of isotonic saline with the three way tap. After five minutes an ampoule (2·83 mg) of the isotope iron-54 was added to a meal as an extrinsic label. The meal consisted of 60 g of cooked lean bacon, one bread roll, and 50 ml of fresh orange juice and had a total non-haem iron content of 3·2 mg.[12,13] The bacon was cooked and the rind removed, and the roll was lightly toasted. The ampoule of ^{54}Fe was emptied into the centre of the bread roll as this was the bulkiest component of the meal.[14,15] The bacon roll was eaten together with the 50 ml of fresh orange juice (25 mg of vitamin C). The exact quantity of isotope given either orally or intravenously was calculated by weighing the ampoules before and after administration, and no food, tea, or coffee was allowed for at least two hours thereafter. Eleven blood samples (8 ml) were taken during the 10 hours after the intravenous injection, and the serum was frozen until assayed.

ISOTOPE ANALYSIS

The isotopes of iron in each serum sample were measured with inductively coupled plasma mass spectrometry.[10] The ratios for the intravenously and orally given isotopes were expressed by the ratio of ^{57}Fe:^{56}Fe and ^{54}Fe:^{56}Fe, respectively—for example, the basal ratio ^{57}Fe:^{56}Fe is 0·024, and 15 minutes after injection the ratio might be 0·100, an enrichment of 0·076. The serum enrichments in ratios were plotted against time,[16] and the areas under these curves were calculated by the trapezoidal rule. The area between the last sample time and the resumption of a basal ratio was extrapolated from the final enrichment and an estimate (over 10 hours) of the elimination rate constant. The amount of the orally absorbed isotope was calculated with the formula as previously described[10]:

$$\text{oral absorption} = \frac{\text{dose (intravenous)} \times \text{area under curve (oral)}}{\text{area under curve (intravenous)} \times \text{dose (oral)}}$$

The coefficient of variation of the ratio ^{54}Fe:^{56}Fe was 1·8% within an assay and 4·7% averaged over 10 assays and of the ratio ^{57}Fe:^{56}Fe was 2·4% and 4·6% respectively.

ANAEMIA AND IRON DEFICIENCY

Subjects were deemed to have iron deficiency anaemia during pregnancy if the haemoglobin concentration was < 110 g/l and associated with a fall in mean cell volume from early pregnancy of more than 6 fl or a rise in zinc protoporphyrin concentration to above the normal range of 3·0 μg/g haemoglobin. The 95% confidence interval of the normal mean drop in mean cell volume by the third trimester was 5·6 fl. Subjects developing microcytosis during pregnancy or raised zinc protoporphyrin concentration but with a normal haemoglobin concentration were regarded as having a depletion of stored iron. The serum ferritin concentration was not used to diagnose iron deficiency during pregnancy for the reasons described in the introduction, although it was used initially with the other variables to ensure that only subjects with normal iron concentrations (ferritin > 12 μg/l) were recruited to the study.

STATISTICS

Results are given as the mean and standard deviation or mean difference and 95% confidence intervals; for serum ferritin concentration and iron absorption the geometric mean and 95% confidence intervals were considered more appropriate. Serial data during pregnancy were compared with analysis of variance and the paired *t* test. Linear correlation was calculated between the log absorption estimates and the log serum ferritin concentrations and other haematological variables.[13]

TABLE I—*Percentage of non-haem iron absorbed from food during normal pregnancy in 12 healthy subjects. 95% Confidence intervals are given in parentheses*

	Weeks of gestation			
Subject No	12	24	36	After delivery
1	3·1	16·1	71·5	36·8
2	3·4	23·3	59·4	
3	4·3	27·4	72·1	15·3
4	4·7	53·0	83·6	5·2
5	5·0	20·0	38·8	
6	5·7	44·1	70·5	15·8
7	6·2	37·1	73·9	4·9
8	12·8	52·7	80·9	
9	14·2	51·3	85·9	19·3
10	14·4	46·4	49·3	13·4
11	14·9	44·2	68·9	4·7
12	16·2	54·4	63·9	
Geometric mean	7·2 (4·9 to 10·9)	36·3* (27·6 to 47·3)	66·1* (57·1 to 76·2)	11·3 (6·0 to 21·2)

*Mean was significantly (P < 0·001) higher than preceding value.

Results

Table I shows the dramatic serial changes in the measurements of absorption, with subjects ordered according to initial absorption. The mean absorption of iron at 24 weeks' gestation was five times higher than that at 12 weeks; it then doubled again and by 36 weeks was 9·1 times (95% confidence interval 6·0 to 13·7) the mean absorption at 12 weeks. The absorption of iron after delivery decreased to levels not significantly different from those found in early pregnancy. Other ferrokinetic data included the mean time taken from administration of the oral isotope to maximal enrichment in serum (163 min (SD 37)) and the mean serum half time of injected iron isotope over the first two hours (86 (25)), which showed no significant (P > 0·05) variation between tests.

Table II shows the changes in the haemoglobin, serum ferritin, and red cell zinc protoporphyrin concentrations and mean cell volume. Between 12 and 24 weeks significant falls occurred in the mean haemoglobin concentration (mean difference 10 g/l (95% confidence interval 0·4 g/l to 1·6 g/l; P < 0·01)) and serum ferritin concentration (P = 0·001). Between 24 and 36 weeks a significant change occurred in ferritin concentration (P < 0·05) and mean cell volume (2·3 fl (0·4 to 4·2 fl; P < 0·05)). After delivery only the mean cell volume was significantly lower than the 12 week value (4·1 fl (2·6 fl to 5·6 fl; P = 0·001)). One subject (subject 4), whose ferritin concentration was 55 μg/l at 12 weeks, showed a fall in her mean cell volume from

TABLE II—*Haematological changes during normal pregnancy in 12 healthy subjects. Means (SD) are given for haemoglobin, mean cell volume, and zinc protoporphyrin and geometric means (95% confidence interval) for ferritin*

	Haemoglobin (g/l)				Mean cell volume (fl)				Zinc protoporphyrin (μg/g Hb)				Ferritin (μg/l)			
	Weeks of gestation				Weeks of gestation				Weeks of gestation				Weeks of gestation			
Subject No	12	24	36	After delivery	12	24	36	After delivery	12	24	36	After delivery	12	24	36	After delivery
1	133	117	110	125	89·0	87·6	85·6	85·0	2·2	2·1	2·9	2·8	93	12	5	15
2	134	115	123		88·8	91·3	92·3		1·7	2·7	2·0		102	64	11	
3	125	105	118	114	89·0	86·5	85·5	81·2	1·8	2·0	2·0	2·7	42	36	5	6
4	115	117	111	121	91·3	91·0	82·4	86·2	1·8	1·7	1·9	1·6	55	7	5	46
5	110	107	118		88·2	91·0	89·9		1·6	2·2	2·0		74	14	7	
6	125	115	109	132	89·5	89·6	86·1	85·7	2·0	2·0	2·8	2·3	25	15	4	21
7	114	118	111	127	86·6	88·2	87·2	85·0	1·8	1·8	1·5	1·2	27	10	5	39
8	130	109	103		83·0	85·3	77·4		1·8	2·2	3·2		86	5	5	
9	126	115	115	125	89·6	89·7	90·7	88·0	2·8	2·2	2·2	2·0	21	5	5	30
10	133	124	124	134	95·8	91·2	90·4	92·0	1·2	1·6	2·0	2·1	25	5	5	35
11	130	132	116	132	93·0	95·6	92·2	90·0	2·2	2·1	2·7	1·1	40	14	5	51
12	142	125	128		92·4	92·5	90·3		1·3	2·6	2·2		25	5	5	
Mean	127	116**	116	126**	89·9	89·9	87·7*	86·6	1·8	2·1	2·3	1·9	43·8	11·1***	5·4*	25·6**
	(9)	(8)	(7)	(7)	(3·4)	(2·8)	(4·6)	(3·3)	(0·4)	(0·3)	(0·7)	(0·6)	(30·1 to 63·7)	(6·6 to 18·7)	(4·6 to 6·3)	(14·3 to 45·5)

Mean was significantly different from preceding value: *($P<0·05$); **($P<0·01$); ***($P<0·001$).

91·0 fl at 24 weeks to 82·4 fl at 36 weeks, while her haemoglobin concentration changed from 117 g/l to 111 g/l and zinc protoporphyrin concentration remained unchanged. She could be regarded as having had depletion of stored iron (iron deficient erythropoeisis) without anaemia. Another subject (subject 8) fulfilled our criteria for iron deficiency anaemia: at 12, 24, and 36 weeks her mean cell volumes were 83·0, 85·3, and 77·4 fl respectively; haemoglobin concentrations 130, 109, and 103 g/l respectively; and ferritin concentrations 86, 5, and 5 μg/l respectively, with a zinc protoporphyrin concentration at 36 weeks of 3·2 μg/g haemoglobin. The absorption profiles of these subjects did not differ from those of the other subjects, who had haematological variables within the normal ranges on all occasions (table I).

A significant correlation existed between ferritin concentrations and iron absorption at 12 weeks' gestation ($r=-0·58$; $P<0·05$), at 24 weeks ($r=-0·64$; $P<0·05$), and after delivery ($r=-0·64$; $P<0·05$) but not at 36 weeks ($r=0·46$; $P>0·05$). The relation between the change in the serum ferritin concentration and the increase in the absorption of iron at any gestational age, however, was not significant. No significant relations existed between any of the other haematological variables and either the absolute value or the change in the absorption of iron during pregnancy.

Discussion

The total iron requirement for a normal singleton pregnancy has been estimated at 800 mg (range 500 to 1400 mg).[3,17,18] The average diet of British women provides about 12 mg of non-haem iron a day.[19-21] For iron balance in early pregnancy only the basal iron requirement (0·8 mg/day) or 6% of the daily iron intake is required. Extra iron (300 mg) is required for the expansion of red cell mass in the second trimester, and further iron (300 mg) is needed for the developing fetus and placenta, especially in the third trimester. If no change in iron stores is assumed then the daily absorption of dietary iron would need to increase from 6% to 32% (3·8 mg/day) over the remaining 28 weeks of pregnancy. This study has shown that absorption in excess of this occurs, which suggests that the increased iron demands of pregnancy could be met without the need for routine supplements.

The haematological variables showed that iron deficiency did not develop in all the subjects; iron deficiency cannot, therefore, be the cause of the increase in absorption seen in all the subjects. The absorption of iron was significantly correlated with the serum ferritin concentration (a recognised indicator of iron stores in women who are not pregnant) at 12 and 24 weeks, although this correlation was not evident at 36 weeks, when the ferritin concentration was at a similar minimum value in all but one subject. No significant correlation existed, however, between the increase in the absorption of iron and the change in ferritin concentration at any time during pregnancy, which suggested that, while the absolute amount of stored iron may have influenced the amount of iron that was absorbed, the change in the amount of iron in the body was not the stimulus for increased absorption. While the fall in the concentrations of haemoglobin and ferritin between the first and second trimesters was accompanied by a fivefold increase in the absorption of iron, between the second and third trimesters the absorption of iron was further doubled while the haemoglobin concentration remained unchanged and the ferritin concentration fell in only half of the subjects. Animal studies have shown that when rats are given iron supplements during pregnancy the total amount of iron in their liver does not change but the haemoglobin concentration still falls and the absorption of iron still rises.[22]

The validity of measuring the absorption of non-haem iron with one stable isotope to label extrinsically the "common pool" of such iron in a meal while another stable isotope is given intravenously has been addressed in a previous study.[23] The label mixed with the food and delayed the time to maximal enrichment of the serum after absorption. The average time to maximal oral enrichment (just under three hours) was more than double the time to maximal oral enrichment estimated in earlier work that measured the absorption of aqueous iron during pregnancy (66 min (SD 21)).[10]

BIOAVAILABILITY

We ensured that our meal provided non-haem iron of "intermediate bioavailability"—that is, the meal contained 30-90 g of meat and 25-75 mg of ascorbic acid.[18,24] Furthermore, the bran in the bread was likely to inhibit to some extent the absorption of iron. Recent work has confirmed that the absorption of iron from such a meal of "average bioavailability" reasonably reflects the degree of absorption from the whole diet.[25] Some of the other inhibitors of absorption of iron—for example, tea or coffee—that might normally be consumed with such a meal were excluded in our study; these inhibitors would have reduced absorption to an extent similar to that which occurs in women who are not pregnant. Tea has been found to reduce the absorption of iron from a breakfast to less than half of that from a breakfast with coffee, but orange juice increased absorption two and a half times.[26] Although the absorption from our meal, therefore, might have been reduced by as much as a third if tea had been included, the increase in absorption would still have been large enough to balance the calculated needs.

The only other serial study of the absorption of iron

Clinical implications

- Uncertainty over the normal physiological adaptations occurring during pregnancy have complicated the issue of whether routine iron supplements are needed
- In this study the mean absorption of non-haem iron from food was 66% at 36 weeks' gestation, an increase of nine times the absorption at 12 weeks' gestation
- The increase in the absorption of iron was not the result of anaemia during pregnancy
- The increase in the absorption of iron from food should be sufficient to meet the increased requirements of pregnancy if the dietary intake is adequate
- Intervention to increase iron concentrations should be limited to advice on dietary intake

from food during pregnancy also found a 10-fold increase, though mean absorption was only 14·6% (SE 1·3) in late pregnancy.[15] The authors of that study and other authors suggested that the absorption of iron from food could not be sufficiently increased during pregnancy to meet demand.[7 15 17 18 27] In the serial study the absorption of non-haem iron was measured from a puréed meal of sausage, fish, cereals, eggs, milk, vegetables, and fruit.[15] At 12 weeks' gestation the absorption from this meal was only 1·5% (0·4), one twelfth of the absorption (18%) from the 3 mg of aqueous iron that was given to women of the same gestational age. This suggests that the meal that was used to assess absorption during pregnancy was one of low bioavailability. Further evidence for the inhibitory nature of this mixed meal was that in another group of 10 pregnant women at 12 weeks' gestation the same authors measured a mean absorption of 5·1% from a hamburger-type meal, the model for the meal used in our study (which gave 7·2% absorption).

The changes in the plasma that result from iron deficiency—that is, low transferrin saturation and low serum ferritin and iron concentrations—are the same changes that occur physiologically during pregnancy and are due to increased plasma volume, increased synthesis of transferrin, and some unidentified factor that depresses ferritin concentrations. The intestinal mucosal cells therefore get the same message: the body requires more iron and absorption should be increased, although how this happens is unknown. In two women in our study the message was received and absorption was increased, yet evidence of iron deficiency ensued. This suggests that iron deficiency anaemia in people with normal stores in early pregnancy and a normal diet may result from a defect in the metabolism of absorbed iron, and while this process could perhaps be overcome with large doses of iron supplements, studies on the fate of absorbed iron would be useful.

CONCLUSION

We conclude that pregnancy stimulates the absorption of iron and that in healthy women who eat an average diet this increase will balance the increased demands of pregnancy without the need for supplements. Prophylactic iron supplements taken during normal pregnancy have never been shown to offer any clinical benefit[28 29]; on the contrary, growing evidence exists that iron supplementation may be harmful. Iron supplementation results in the inhibition of the absorption of zinc from the intestine.[30-32] Fatal iron overdose has occurred in children who have ingested the colourful supplements that are often prescribed—at a substantial cost to the NHS—but not used.[33 34] We recommend that intervention to increase iron concentrations in pregnant women should consist of simple dietary advice that encourages the optimal consumption of available dietary iron.

This study was supported by grants from the Medical Research Council, the Natural Environmental Research Council, Action Research for the Crippled Child, and the Sir Jules Thorn Charitable Trust.

1 Hibbard BM. Iron and folate supplements during pregnancy: supplementation is valuable only in selected patients. *BMJ* 1988;**297**:1324-6.
2 Horn E. Iron and folate supplements during pregnancy: supplementing everyone treats those at risk and is cost effective. *BMJ* 1988;**297**:1325-7.
3 Lind T. Iron supplementation during pregnancy. In: Campbell DM, Gillmer MD, eds. *Nutrition during pregnancy*. London: Royal College of Obstetricians and Gynaecologists, 1983:181-91.
4 Hytten FE. Blood volume changes in normal pregnancy. *Clinics in Haematology* 1985;**14**:601-12.
5 Taylor DJ, Mallen C, McDougall N, Lind T. Effect of iron supplementation on serum ferritin levels during and after pregnancy. *Br J Obstet Gynaecol* 1982;**89**:1011-7.
6 World Health Organisation. Nutritional anaemias. Report of a WHO group of experts. *WHO Tech Rep Ser* 1972;**503**:29-50.
7 Institute of Medicine (US) Subcommittee on Dietary Intake and Nutrient Supplement during Pregnancy. Iron nutrition during pregnancy. In: *Nutrition during pregnancy*. Washington: National Academy Press, 1990: 272-98.
8 Hahn PF, Carothers EL, Darby WJ, Martin M, Sheppard CW, Cannon ROY. Iron metabolism in early pregnancy as studied with the radioactive isotope Fe59. *Am J Obstet Gynecol* 1951;**61**:477-86.
9 Heinrich HC. Intestinal iron absorption in man—methods of measurement, dose relationships, diagnostic and therapeutic applications. In: Hallberg L, Harwerth HG, Vannoti A, eds. *Iron deficiency. Pathogenesis. Clinical aspects. Therapy*. London: Academic Press, 1970:213-6.
10 Whittaker PG, Lind T, Williams JG. Iron absorption during normal human pregnancy: a study using stable isotopes. *Br J Nutr* 1991;**65**:457-63.
11 Commission on atomic weights and isotopic abundances. Isotopic composition of the elements 1989. *Pure and Applied Chemistry* 1991;**63**:991-1002.
12 Paul AA, Southgate DAT. *McCance and Widdowson's the composition of foods*. 4th ed. London: HMSO, 1978.
13 *Geigy scientific tables*. 8th ed. Basle: Ciba-Geigy, 1981.
14 Bjorn-Rasmussen E, Hallberg L, Magnusson B, Rossander L, Svanberg B, Arvidsson B. Measurement of iron absorption from composite meals. *Am J Clin Nutr* 1976;**26**:1311-9.
15 Svanberg B, Arvidsson B, Bjorn-Rasmussen E, Hallberg L, Rossander L, Swolin B. Dietary iron absorption in pregnancy—a longitudinal study with repeated measurements of non-haem iron absorption from the whole diet. *Acta Obstet Gynecol Scand* 1975;**48**(suppl):43-86.
16 Gibaldi M, Perrier D. *Pharmacokinetics*. New York: Marcel Dekker, 1982: 145-98.
17 Pritchard JA, Scott DE. Iron demands during pregnancy. In: Hallberg L, Harwerth HG, Vannoti A, eds. *Iron deficiency. Pathogenesis. Clinical aspects. Therapy*. London: Academic Press, 1970:173-83.
18 Bothwell TH, Charlton RW, Cook JD, Finch CA. *Iron metabolism in man*. Oxford: Blackwell, 1979.
19 Black AE, Wiles SJ, Paul AA. The nutrient intakes of pregnant and lactating mothers of good socio-economic status in Cambridge, UK: some implications for recommended daily allowances of minor nutrients. *Br J Nutr* 1986;**56**:59-72.
20 Schofield C, Stewart J, Wheeler E. The diets of pregnant and post-pregnant women in different social groups in London and Edinburgh: calcium, iron, retinol, ascorbic acid, and folic acid. *Br J Nutr* 1989;**62**:363-77.
21 Darke SJ, Diselduff MM, Try GP. Frequency of mean daily intakes of food energy and selected nutrients obtained during nutrition surveys of different groups of people in Great Britain. *Br J Nutr* 1980;**44**:243-52.
22 Southon S, Wright AJ, Fairweather-Tait SJ. The effect of differences in dietary iron intake on ^{59}Fe absorption and duodenal morphology in pregnant rats. *Br J Nutr* 1989;**62**:707-17.
23 Barrett JFR, Whittaker PG, Williams JG, Fenwick JD, Lind T. The comparison of stable and radioisotopes in the measurement of iron absorption in healthy women. *Clin Sci* (in press).
24 Monsen ER, Hallberg L, Layrisse M, Hegsted DM, Cook JD, Mertz W, *et al.* Estimation of available dietary iron. *Am J Clin Nutr* 1978;**31**:134-41.
25 Cook JD, Dassenko SA, Lynch SR. Assessment of the role of nonheme-iron availability in iron balance. *Am J Clin Nutr* 1991;**54**:717-22.
26 Rossander L, Hallberg L, Bjorn-Rasmussen E. Absorption of iron from breakfast meals. *Am J Clin Nutr* 1979;**32**:2484-9.
27 Department of Health and Social Security. *Recommended daily amounts of food energy and nutrients for groups of people in the United Kingdom*. London: HMSO, 1979. (Report No 15.)
28 Hemminiki E, Starfield B. Routine administration of iron and vitamins during pregnancy: a review of controlled clinical trials. *Br J Obstet Gynaecol* 1978;**85**:404-10.
29 US Preventive Services Task Force. Routine iron supplementation during pregnancy. Policy statement and review article. *JAMA* 1993;**270**:2846-54.
30 Ramdath DD, Golden MHN. Non-haematological aspects of iron nutrition. *Nutrition Research Reviews* 1989;**2**:29-49.
31 Crofton RW, Gvaozdanovic D, Khin CC, Brunt PW, Mowat N, Aggett PJ. Inorganic zinc and the intestinal absorption of ferrous iron. *Am J Clin Nutr* 1989;**50**:141-4.
32 Hambidge KM, Krebs NF, Sibley L, English J. Acute effects of iron therapy on zinc status during pregnancy. *Obstet Gynecol* 1987;**70**:593-6.
33 Reynolds LG, Klein M. Iron poisoning—a preventable hazard of childhood. *S Afr Med J* 1985;**67**:680-3.
34 Bonnar J, Goldberg A, Smith JA. Do pregnant women take their iron? *Lancet* 1967;**i**:457-8.

(Accepted 18 April 1994)