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Maternal intake of antioxidant vitamins in pregnancy in relation to maternal and fetal plasma levels at delivery

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The aim of the present study was to test the hypothesis that maternal intake of antioxidant vitamins is associated with maternal and cord plasma levels at delivery. Women were recruited in early pregnancy in Aberdeen Maternity Hospital and habitual diet during pregnancy was assessed by a food-frequency questionnaire mailed at 34 weeks gestation. Blood samples were taken at recruitment (*n* 1149) and maternal (*n* 1149) and cord blood samples (*n* 747) taken at delivery for analyses of vitamins A, C, E and β-carotene. Maternal plasma levels of vitamin E and β-carotene at delivery were significantly higher than levels in early pregnancy while levels of vitamins A and C were significantly lower. Positive correlations were observed for maternal levels of all the vitamins between early pregnancy and delivery. At delivery, maternal plasma concentrations of vitamins A, E and β-carotene were significantly higher than cord levels, while maternal levels of vitamin C were significantly lower. There were significant correlations between maternal and cord plasma concentrations for β-carotene and vitamin C but not for vitamins A or E. Maternal dietary intakes were positively correlated with maternal plasma levels of vitamins C, E and β-carotene in early pregnancy, with maternal plasma levels of β-carotene and vitamin C at delivery and with cord plasma levels of β-carotene and vitamin C. The results from the present study show that, in this population, maternal diet influences cord plasma levels of β-carotene and vitamin C, but not vitamins A and E.

Antioxidants: Vitamins: Diet: Pregnancy

During pregnancy mothers are advised to eat well on the assumption that nutrients from the maternal diet will be transferred to the fetus for growth and development (Food Standards Agency, 2004). Antioxidant vitamins E, A, C and β-carotene are essential nutrients and therefore supply to the fetus must come from the maternal circulation *via* placental transfer (James & Stephenson, 1998). Although several studies have investigated the plasma status of one or some of these antioxidant vitamins (predominantly vitamin E) during pregnancy and/or have made comparisons between maternal and cord levels (Haga *et al.* 1982; Chen *et al.* 1996; Oostenbrug *et al.* 1998; Yeum *et al.* 1998; Bolisetty *et al.* 2002*a*,*b*), few studies have explored the relationship between maternal dietary intakes of these vitamins and levels seen in cord plasma. One study has investigated the effect maternal dietary intakes have on cord plasma levels at birth but only for vitamin E and β-carotene (Keily *et al.* 1999).

As part of a large cohort study, we had the opportunity of looking at dietary and plasma levels of vitamins E, A, C and β-carotene in a large group of mothers and their babies. The aim of the present study was to investigate the effect of maternal diet on maternal blood at booking and delivery and on cord blood levels in a large population of pregnant women to test the hypothesis that maternal dietary intake of antioxidant vitamins is associated with cord plasma levels of these vitamins.

Methods

Subjects

The present study was part of the ‘Study of Eczema and Asthma To Observe the influence of Nutrition’ Study, known as the SEATON Study, which was designed to investigate the influence of maternal diet during pregnancy on the subsequent incidence of childhood asthma and allergies (Martindale *et al.* 2005). Subjects were recruited at their booking visit in early pregnancy (range 5–35 weeks; median 12 weeks; interquartile range 11–13 weeks) at Aberdeen Maternity Hospital (Aberdeen, UK) antenatal clinics from October 1997 to April 1999 by research nurses. The only criterion for exclusion was insulin-dependent diabetes. The 2000 women recruited were similar to the rest of the obstetric population of the Grampian region during the recruitment period (Martindale *et al.* 2005). Of 2000 women recruited, 1924 had live singleton births. Of these women who had singleton births, 1149 provided blood suitable for analyses both at recruitment and delivery and were included in the present

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Abbreviation: FFQ, food-frequency questionnaire.

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study. Cord blood samples, suitable for analyses, were obtained from the babies of 747 of the 1149 subjects. The 1149 subjects were not significantly different from the rest of the 2000 women in relation to age at delivery, height and weight at recruitment, husband or partner's social class, maternal smoking habit, gestation at booking and gestation at delivery. Table 1 shows a descriptive profile of the subjects.

Dietary assessment

Habitual maternal diet during pregnancy was assessed with the Scottish Collaborative Group 150-item semi-quantitative food-frequency questionnaire (FFQ), version 5.4, which was developed and validated for use in Scottish populations. In a separate validation study of forty women, the correlation coefficients between intakes by FFQ and 4 d weighed record were 0·34 ($P<0·05$) for vitamin A, 0·44 ($P<0·01$) for β-carotene, 0·52 ($P<0·001$) for vitamin E and 0·59 ($P<0·001$) for vitamin C (Masson *et al.* 2003). The FFQ was mailed to subjects at 34 weeks gestation for completion and enquired about all major food groups and supplements consumed over the previous 2–3 months. The data from the FFQ were analysed using McCance and Widdowson's UK food composition tables (Holland *et al.* 1991). Vitamin intake from supplements consumed in later pregnancy was also estimated.

Sample collection

Blood samples were taken at recruitment and both maternal and cord blood samples were taken at delivery by labour ward staff when possible. In each case, 10 ml blood were drawn into a sodium heparin vacutainer tube for separating plasma and stored at 4°C until processed. All samples were processed within 20 h of sampling and plasma samples were stored at −70°C until required for vitamin analyses. Before storage, an equal volume of metaphosphoric acid (10 %) was added to plasma samples designated for vitamin C analysis in order to deproteinise the plasma and stabilise the vitamin C content.

Table 1. Descriptive characteristics of the subjects from whom blood suitable for analysis was obtained both at booking and delivery (*n* 1149)
(Mean values and standard deviations)

Descriptive characteristics	*n*	Mean	SD	Range
Maternal age at delivery (years)*	1138	29·4	5·55	15–44
Maternal height at booking (cm)†	1148	163·1	6·41	142–184
Maternal weight at booking (kg)‡	1147	67·2	13·36	35–136
Husband or partner's social class (%)§				
Non-manual	427	37·5		
Manual	506	44·4		
Other	206	18·1		
Smoking habit (%)				
Never smoked	626	54·5		
Smoker	523	45·5		
Gestation period at booking (%)‖				
≤20 weeks	1109	97·3		
>20 weeks	31	2·7		
Gestation period at delivery (%)				
≤36 weeks	62	5·4		
37–42 weeks	1087	94·6		

* Data missing for eleven subjects.
† Data missing for one subject.
‡ Data missing for two subjects.
§ Data missing for ten subjects.
‖ Data missing for nine subjects.

Methods of blood analyses

The simultaneous extraction of vitamin E (α-tocopherol), β-carotene and vitamin A (retinol) from thawed maternal and cord plasma samples was carried out using a modified method of Hess *et al.* (1991). Plasma was diluted with an equal volume of water and deproteinised with ethanol containing 0·025 % butylated hydroxytoluene before extraction of vitamins with *n*-hexane. After centrifugation at 13 000 rpm for 5 min at room temperature the resultant upper hexane layer was removed, dried down under vacuum, and reconstituted to the original plasma volume with 1,4 dioxane–hexane (1:1, v/v). The samples were analysed simultaneously for vitamin E, β-carotene and vitamin A by normal-phase HPLC using an Alltech Partisil Si 5 micron (250 mm × 4·6 mm internal diameter) column (Alltech Associates, Deerfield, IL, USA) with hexane and 1,4 dioxane as the mobile phase (Onibi *et al.* 1998). The system was controlled and the data produced by a Varian Star Chromatography Workstation (software version 4.0; Varian Inc., Palo Alto, CA, USA). The vitamin concentrations were calculated by reference to external standards.

Vitamin C concentrations in maternal and cord samples were determined using the automated enzymic procedure developed by Lee *et al.* (1997) for a Roche Cobas Fara centrifugal autoanalyser (F. Hoffmann-La Roche & Co., Basle, Switzerland). Modifications were made to the instrument parameters to suit a Roche Cobas Mira centrifugal autoanalyser in this instance.

Data handling

Data for vitamin E, β-carotene and vitamins A and C, obtained from the dietary questionnaire and blood analyses, were combined with maternal age, weight, height, gestational age at booking and delivery, maternal smoking habit, husband or partner's social class and delivery type from the Aberdeen Maternity and Neonatal Databank. Maternal smoking habit was assessed at booking and for the present study non-smokers refer to women who had never smoked and smokers refer to women who had ever smoked. For the variable 'Husband or partner's social class' the category 'Other' relates to women who did not have a partner or whose partner was unemployed. Delivery type was categorised into those who laboured and those who did not (elective caesarean sections).

Statistical analysis

Before statistical analyses, results for late bookers (those who booked after 20 weeks (*n* 31)) and pre-term deliveries (those who delivered before 37 weeks (*n* 62)) were eliminated where appropriate. Reasons for eliminating these groups were that in late pregnancy some of the blood vitamin levels differed from those seen in early pregnancy (results not shown) and the group who delivered preterm were more likely to have problem pregnancies, their newborns to have problems of prematurity and thus the blood results to be different from term deliveries. In addition, results for subjects for whom the gestational age at booking was missing (*n* 9) were also eliminated. This resulted in 1050 subjects whose results at booking and delivery could be compared and 716 subjects whose maternal and cord results could be compared at delivery. Differences between mean maternal plasma vitamin concentrations at booking and delivery and between mean maternal and cord concentrations at delivery were assessed by paired *t* test. Before carrying out the *t* test, the blood variables were checked for normal distribution by the Kolmogorov–Smirnov test and geometric means were calculated for $\log_{10}$-transformed variables (maternal and cord blood β-carotene).

Dietary vitamin intake was combined with supplement intake to provide total vitamin intake for analyses. Univariate ANOVA was used to compare differences between total vitamin intakes, maternal blood levels of vitamins at booking and delivery and cord blood concentrations of vitamins within non-smoking and smoking groups, within manual and non-manual groups, and within labour and no-labour groups, each group being adjusted for the other two groups. Geometric means were calculated for $\log_{10}$-transformed variables (total dietary intake values and β-carotene blood concentrations). Total vitamin intake was adjusted for energy by calculating residuals in a regression model where the vitamin intake was the dependent variable and the total energy intake the independent variable. Partial correlation analysis was used to investigate the relationships between total dietary intakes (adjusted and unadjusted for energy) with maternal plasma levels at booking and at delivery and with cord plasma levels of the vitamins studied, adjusting for smoking, social class and the effect of labour. All statistical analyses were performed using SPSS version 11.5 (SPSS Inc., Chicago, IL, USA).

Results

Table 2 displays the intake of vitamins from diet and supplements. As FFQ may overestimate absolute levels of nutrient intake, the data for dietary intake should be interpreted with caution, but for vitamin A the mean was below the reference nutrient intake for pregnancy of 700 μg/d while for vitamin C the mean intakes were considerably higher than the reference nutrient intake for pregnancy of 50 mg/d (Department of Health, 1991).

Maternal plasma levels of vitamin E and β-carotene at delivery were significantly higher and levels of vitamins A and C at delivery were significantly lower than those levels at booking. β-Carotene showed the strongest significant correlation between booking and delivery (Table 3).

At delivery, plasma concentrations of vitamin E, β-carotene and vitamin A were significantly higher in mothers than in the cord blood of their babies. By contrast, maternal plasma vitamin C levels at delivery were significantly lower than cord levels. There were highly significant correlations between maternal and cord concentrations of β-carotene and vitamin C but only weak correlations were seen for vitamins E and A (Table 4).

Comparisons between subgroups of subjects based on smoking status, manual *v.* non-manual social class and labour *v.* elective caesarean section are shown in Tables 5, 6 and 7. Mothers who had ever smoked had a significantly lower vitamin C intake, significantly lower plasma levels of all the vitamins apart from vitamin A at delivery and significantly lower levels of β-carotene in the cord blood of their babies compared with mothers who had never smoked. Compared with the non-manual group, mothers in the manual group had a significantly lower vitamin C intake, significantly lower plasma levels of β-carotene, vitamin A and vitamin C at booking, significantly lower plasma levels of β-carotene at delivery and significantly lower cord plasma levels of vitamin E. Significant differences between the group who laboured and those who did not were only observed in maternal and cord blood at delivery. At delivery, those mothers who did not labour had significantly lower blood levels of vitamins E and A and significantly higher levels of vitamin C. This pattern was also observed in the cord blood of their babies.

Table 2. Vitamin and energy intake for subjects from whom blood suitable for analysis was obtained both at booking and delivery (*n* 1149)

(Mean values and standard deviations)

Variable	*n*	Mean	SD
Dietary vitamin E (mg/d)*	1065	8·05	3·18
Vitamin E supplements (mg/d)†	1053	1·34	9·08
Total vitamin E (mg/d)†	1053	9·7	9·67
Dietary β-carotene (μg/d)*	1065	2302	1861·6
β-Carotene supplements (μg/d)†	1053	90·88	591·67
Total β-carotene (μg/d)†	1053	2394	2001·17
Dietary vitamin A (μg/d)*	1065	555·4	600·58
Vitamin A supplements (μg/d)†	1053	100·84	890·45
Total vitamin A (μg/d)†	1053	655·7	1062·3
Dietary vitamin C (mg/d)*	1065	126·9	64·46
Vitamin C supplements (mg/d)†	1053	10·10	42·89
Total vitamin C (mg/d)†	1053	136·7	80·34
Energy (kJ/d)*	1065	10 655	3603

* Data unavailable for eighty-four subjects.

† Data unavailable for ninety-six subjects.

In light of the differences found in Tables 5, 6 and 7, adjustments were made for smoking, social class and the effect of labour before carrying out partial correlation analysis on maternal total dietary intake with maternal and cord blood concentrations (Table 8). There were significant positive correlations between maternal dietary intake and maternal blood at booking for all vitamins. At delivery, β-carotene and vitamin C exhibited significant positive correlations. In the case of vitamin E, the correlation was only significant when diet was energy-adjusted. When maternal dietary intake was correlated with cord blood at delivery, only β-carotene and vitamin C exhibited significant positive correlations. We investigated results for lipid-adjusted vitamin E (results not shown) and found that adjusting for lipids (triacylglycerol + cholesterol) did not alter the significances observed for vitamin E.

Discussion

Dietary intake of vitamins

Although a direct comparison of dietary intakes between studies is difficult to make as the methods for dietary assessment and food composition databases used are often different, dietary intakes of the vitamins studied were broadly

Table 3. The relationship between maternal plasma vitamin levels at booking and delivery (*n* 1050; late bookers and preterm deliveries eliminated)

(Mean values and 95 % confidence intervals)

		Booking (μmol/l)		Delivery (μmol/l)				
	n	Mean	95 % CI	Mean	95 % CI	*P*	Correlation	*P*
Vitamin E	1048	23·3	22·94, 23·74	31·6	31·07, 32·12	<0·001	0·341†	<0·001
log$_{10}$ β-Carotene	1047	0·48*	0·46, 0·50	0·60*	0·58, 0·62	<0·001	0·563‡	<0·001
Vitamin A	1048	1·40	1·38, 1·42	1·31	1·29, 1·32	<0·001	0·238†	<0·001
Vitamin C	1007	68·41	66·70, 70·13	36·96	35·80, 38·12	<0·001	0·262‡	<0·001

* Geometric mean.

† Spearman's correlation.

‡ Pearson's correlation.

similar to those reported in other pregnant women in the UK (Keily *et al.* 1999; Mathews *et al.* 1999). The mean value for the total dietary intakes of vitamin C was higher than the UK reference nutrient intake for pregnancy of 50 mg/d and the US recommended intake of 85 mg/d. For vitamin A the mean intake was below the UK reference nutrient intakes for pregnancy (700 μg/d) and the US reference nutrient intakes for pregnancy (770 μg/d). For vitamin E there are no reference nutrient intakes in the UK, although Black *et al.* (1986) reported that intakes of 3·8 to 6·2 mg/d for vitamin E appeared to be satisfactory for pregnant and lactating women, while in the USA intakes of 15 mg/d are recommended during pregnancy. There are no reference nutrient intakes for β-carotene in either the UK or the USA. In the present study 69 % of subjects had intakes of vitamin A less than 700 μg/d, with 25 % having intakes less than the lower reference nutrient intake of 350 μg/d. For vitamin E, 3 % of subjects had intakes of less than 3·8 mg/d but 78 % had intakes below 15 mg/d, while for vitamin C only 5 % had intakes below 50 mg/d. There were no significant differences in cord plasma levels of vitamins A and E in infants whose mothers had intakes below 700 μg/d or 15 mg/d respectively but cord plasma vitamin C was significantly lower in infants whose mothers' intakes were lower than 50 mg/d ($P=0·000$) than in those whose mothers' intakes were above this level.

Maternal vitamin levels during pregnancy

Although the mean maternal plasma concentrations of vitamins E and A in early pregnancy were similar to those in other studies (Oostenbrug *et al.* 1998; Keily *et al.* 1999), the β-carotene mean plasma concentration in the present study was higher when compared with that reported by Keily *et al.* (1999). This could be due to the geometric mean being expressed in the present study as our data for β-carotene was normalised by log$_{10}$-transformation. Information for vitamin C levels in early pregnancy is scarce and we could not find a study to compare our mean level with. We found mean values of vitamins A, C and β-carotene in maternal plasma to be above non-pregnant serum cut-off point values for marginal deficiency of vitamin A (1·05 μmol/l; Haskell & Brown, 1999), vitamin C (17 μmol/l (3 mg/l); Gibson, 1990) and β-carotene (0·22 μmol/l; Wondmikun, 2004). For vitamin A, 16 % (in early pregnancy) and 29 % (at delivery) of our subjects had plasma levels less than 1·05 μmol/l. For β-carotene, 14 % (in early pregnancy) and 4 % (at delivery) of our subjects had plasma levels less than 0·22 μmol/l and for vitamin C, 3 % (in early pregnancy) and 4 % (at delivery) of our subjects had levels below 17 μmol/l. We found that cord blood levels of vitamins A, C and β-carotene in the infants of mothers whose blood levels were below the cut-off values were significantly lower ($P=0·007$, $P=0·000$ and $P=0·000$ respectively) than cord blood levels in infants whose mothers' blood levels were above the cut-off values. The normal adult range for non-pregnant blood levels of vitamin E is 18·6–34·0 μmol/l (Jacobs, 1990), into which range the mean value of vitamin E for our subjects falls (20 % (in early pregnancy) and 4·7 % (at delivery) of our subjects had plasma vitamin E levels which were less than 18·6 μmol/l and cord plasma levels in the babies of these women were not different from those whose levels were above18·6 μmol/l).

At delivery the maternal plasma levels of all the vitamins were significantly different from the levels at booking, suggesting that physiological changes in vitamin levels occur during pregnancy and/or at delivery. Maternal plasma

Table 4. The relationship between maternal and cord plasma vitamin levels at delivery (*n* 716; preterm deliveries eliminated)

(Mean values and 95 % confidence intervals)

		Maternal (μmol/l)		Cord (μmol/l)				
	n	Mean	95 % CI	Mean	95 % CI	*P*	Correlation†	*P*
Vitamin E	714	31·51	30·88, 32·15	4·30	4·15, 4·37	<0·001	0·068	0·068
log$_{10}$ β-Carotene	710	0·62*	0·59, 0·65	0·017*	0·015, 0·020	<0·001	0·465	<0·001
Vitamin A	710	1·31	1·27, 1·35	0·90	0·88, 0·93	<0·001	0·080	0·032
Vitamin C	684	36·90	35·50, 38·29	92·11	88·94, 95·29	<0·001	0·432	<0·001

* Geometric mean.

† Spearman's correlation.

Table 5. Comparisons between total vitamin intakes, maternal blood levels at booking and delivery and cord blood levels at delivery within smokers and non-smokers (adjusted for social class and the effect of labour)

(Mean values)

	Smokers		Non-smokers		
	n	Mean	*n*	Mean	*P*
Vitamin E					
Maternal intake (mg/d)	430	8·61	572	8·39	0·522
Maternal blood level at booking (μmol/l)	492	22·98	599	23·60	0·239
Maternal blood level at delivery (μmol/l)	486	30·95	582	32·00	0·046
Cord blood level at delivery (μmol/l)	297	4·21	405	4·28	0·576
β-Carotene					
Maternal intake (μg/d)	430	1748	572	1894	0·170
Maternal blood level at booking (μmol/l)	492	0·441	598	0·500	0·051
Maternal blood level at delivery (μmol/l)	486	0·561	582	0·633	0·009
Cord blood level at delivery (μmol/l)	296	0·014	402	0·020	0·012
Vitamin A					
Maternal intake (μg/d)	430	511	572	475	0·107
Maternal blood level at booking (μmol/l)	492	1·39	599	1·41	0·700
Maternal blood level at delivery (μmol/l)	486	1·33	582	1·29	0·425
Cord blood level at delivery (μmol/l)	296	0·88	402	0·92	0·147
Vitamin C					
Maternal intake (mg/d)	430	112	572	124	0·028
Maternal blood level at booking (μmol/l)	483	65·96	587	69·90	0·072
Maternal blood level at delivery (μmol/l)	474	34·49	572	38·34	0·003
Cord blood level at delivery (μmol/l)	286	89·05	398	93·08	0·137

Table 6. Comparisons between total vitamin intakes, maternal blood levels at booking and delivery and cord blood levels at delivery within manual and non-manual social classes (adjusted for smoking and the effect of labour)

(Mean values)

	Manual		Non Non-manual		
	n	Mean	*n*	Mean	*P*
Vitamin E					
Maternal intake (mg/d)	451	8·45	380	8·34	0·382
Maternal blood level at booking (μmol/l)	486	23·17	411	23·82	0·158
Maternal blood level at delivery (μmol/l)	470	31·68	404	31·79	0·328
Cord blood level at delivery (μmol/l)	313	4·09	268	4·35	0·039
β-Carotene					
Maternal intake (μg/d)	451	1774	380	1914	0·429
Maternal blood level at booking (μmol/l)	486	0·431	411	0·548	0·000
Maternal blood level at delivery (μmol/l)	470	0·557	404	0·664	0·000
Cord blood level at delivery (μmol/l)	312	0·015	267	0·020	0·244
Vitamin A					
Maternal intake (μg/d)	451	489	380	468	0·702
Maternal blood level at booking (μmol/l)	486	1·37	411	1·45	0·011
Maternal blood level at delivery (μmol/l)	470	1·33	404	1·29	0·524
Cord blood level at delivery (μmol/l)	312	0·89	267	0·91	0·394
Vitamin C					
Maternal intake (mg/d)	451	114	380	127	0·044
Maternal blood level at booking (μmol/l)	476	67·85	403	71·30	0·002
Maternal blood level at delivery (μmol/l)	464	36·14	395	37·74	0·518
Cord blood level at delivery (μmol/l)	306	92·79	263	87·90	0·138

vitamin E levels at delivery were significantly higher than at booking, as was found by Chen *et al.* (1996). Maternal plasma levels of β-carotene were also significantly higher than at booking, but maternal vitamin A levels were significantly lower at delivery than at booking, in contrast to the findings of Oostenbrug *et al.* (1998) who found no difference. Perhaps the difference between the present study (*n* 1149) and Oostenbrug's study (*n* 35) could be attributed to the difference in sample size. Other than Oostenbrug's study, no other information where vitamin A had been measured in early pregnancy and at delivery in the same women was found. Lachili *et al.* (1999) and Sapin *et al.* (2000) reported a significant decrease in vitamin A concentrations at delivery compared with values for non-pregnant women. Vitamin C levels were also significantly lower at delivery than at booking and tended to be lower in those booking later in pregnancy in

Table 7. Comparisons between total vitamin intakes, maternal blood levels at booking and delivery and cord blood levels at delivery within those who laboured and those who did not (elective caesarean sections) (adjusted for smoking and social class)

(Mean values)

	Labour		No labour		
	n	Mean	*n*	Mean	*P*
Vitamin E					
Maternal intake (mg/d)	926	8·48	76	8·14	0·420
Maternal blood level at booking (μmol/l)	1003	23·31	88	23·47	0·770
Maternal blood level at delivery (μmol/l)	983	31·85	85	27·71	0·000
Cord blood level at delivery (μmol/l)	637	4·30	65	3·76	0·004
β-Carotene					
Maternal intake (μg/d)	926	1815	76	2015	0·232
Maternal blood level at booking (μmol/l)	1002	0·474	88	0·500	0·619
Maternal blood level at delivery (μmol/l)	983	0·603	85	0·552	0·196
Cord blood level at delivery (μmol/l)	634	0·018	64	0·013	0·190
Vitamin A					
Maternal intake (μg/d)	926	479	76	468	0·999
Maternal blood level at booking (μmol/l)	1003	1·40	88	1·40	0·842
Maternal blood level at delivery (μmol/l)	983	1·33	85	1·11	0·000
Cord blood level at delivery (μmol/l)	634	0·91	64	0·83	0·038
Vitamin C					
Maternal intake (mg/d)	926	479	76	468	0·226
Maternal blood level at booking (μmol/l)	985	27·38	85	25·05	0·250
Maternal blood level at delivery (μmol/l)	963	35·99	83	43·60	0·000
Cord blood level at delivery (μmol/l)	620	90·15	64	103·45	0·022

Table 8. Correlations between total vitamin intake and maternal blood at booking and delivery and cord blood at delivery after adjustment for smoking, social class and labour

	n	Correlation*	*P*	Correlation†	*P*
Maternal intake *v.* maternal blood at booking (late bookers eliminated)					
Vitamin E	1002	0·047	0·134	0·130	0·000
β-Carotene	1001	0·205	0·000	0·220	0·000
Vitamin A	1002	0·077	0·015	0·111	0·000
Vitamin C	983	0·198	0·000	0·263	0·000
Maternal intake *v.* maternal blood at delivery (early deliveries eliminated)					
Vitamin E	985	0·048	0·133	0·081	0·012
β-Carotene	985	0·194	0·000	0·265	0·000
Vitamin A	985	0·066	0·038	0·039	0·223
Vitamin C	964	0·172	0·000	0·215	0·000
Maternal intake *v.* cord blood at delivery (early deliveries eliminated)					
Vitamin E	656	−0·026	0·508	−0·027	0·489
β-Carotene	652	0·117	0·003	0·142	0·000
Vitamin A	652	−0·009	0·829	0·047	0·236
Vitamin C	639	0·101	0·011	0·109	0·006

* Total dietary intake unadjusted for energy.
† Total dietary intake adjusted for energy.

line with the findings of Mason & Rivers (1971). Strong positive correlations were observed for all the vitamins between maternal levels at booking and delivery (all $P < 0{\cdot}001$).

Relationship between maternal and fetal vitamin levels

In the present study there was no correlation between vitamin E levels in maternal and cord plasma, consistent with the findings of Cachia *et al.* (1995), Oostenbrug *et al.* (1998) and Yeum *et al.* (1998). In contrast, Leonard *et al.* (1972), Chen *et al.* (1996) and Baydas *et al.* (2002) reported a positive association. We found a highly significant correlation between maternal and cord β-carotene concentrations at delivery, consistent with the findings of Oostenbrug *et al.* (1998), a weak but significant association between maternal and cord plasma vitamin A levels, in contrast to previous studies (Chen *et al.* 1996; Oostenbrug *et al.* 1998), and a significant correlation between maternal and cord plasma vitamin C concentrations, in contrast to the study of Baydas *et al.* (2002). Differences between studies could possibly be attributed to differences in the number and selection of women, gestational age at delivery and perhaps to differences in the habitual diets of women.

Factors affecting dietary intakes and blood levels of vitamins

Cigarette smokers have been reported to have different dietary intakes and tissue levels of most micronutrients (Ross *et al.* 1995; Ortega *et al.* 1998*a*,*b*; Mathews *et al.* 2000). We only found vitamin C intake to be different and, with the exception of vitamin A, all the other vitamin levels were different in maternal blood at delivery. Only vitamin C intake was different between social classes and as adjustment had been made for smoking, this was a social-class effect. In a national UK survey it has been reported that the manual social class had lower consumption of fruit and vegetables (Billson *et al.* 1999), which would account for the lower vitamin C intake. It is not clear why the other nutrients were not affected. As corrections had been made for smoking and the fact that there was no difference in dietary intakes of β-carotene and vitamin A between manual and non-manual groups, we find it difficult to explain why levels of these vitamins were significantly lower in maternal blood at booking in the manual group. In addition, as we had also adjusted for the effects of labour we cannot explain why the level of cord plasma vitamin E should be lower in infants of mothers in the manual group. Our finding that labour affected maternal and cord plasma levels of vitamins

A, E and C at delivery agrees with the findings of Gonzalez-Corbella *et al.* (1998) and Woods *et al.* (2002) for vitamins E and C. They reported that maternal and cord blood levels of vitamin E and vitamin C were significantly higher and lower respectively in women who have laboured when compared with women who have not.

Effect of dietary intake on maternal and cord blood vitamin levels

After adjusting for smoking, social class and the effect of labour, the present study has shown that maternal dietary intake of the essential vitamins A, E, C and β-carotene during pregnancy are associated significantly with maternal blood levels in early pregnancy, with β-carotene and vitamin C showing the strongest correlations (vitamin E only showing a significant correlation when dietary intake was adjusted for energy). In a study of sixty-six women in the Republic of Ireland, Keily *et al.* (1999) found no correlations between dietary intakes of vitamin E and β-carotene (unadjusted for energy) and maternal plasma levels in early pregnancy, in contrast to the present results. However, in Keily's study, not only were dietary intakes unadjusted for energy, but also the sample size was smaller than the present study and no adjustments had been made for smoking and social class.

At delivery the correlation between maternal diet and plasma levels for β-carotene becomes even stronger, but for vitamins A, E and C the correlation becomes weaker, with vitamin A losing significance when dietary intake is adjusted for energy. This suggests that factors other than diet are affecting those plasma vitamin levels. Maternal levels of β-carotene and vitamin C at delivery were strongly associated with cord levels, so it is no surprise to see that maternal dietary intake of these vitamins was significantly correlated with cord levels although the association was weaker than that seen between maternal dietary intake and the maternal plasma levels at delivery. An explanation for no association being found between maternal dietary intake and cord plasma concentrations of vitamins A and E could be that the population of women in the present study was well-enough nourished. Rondo *et al.* (1995) found that when moderate maternal vitamin A deficiency occurs, there tends to be a correlation between maternal and cord blood, whereas when maternal vitamin A deficiency is minimal the correlation disappears. We investigated this possibility in our subjects but found no significant correlation between maternal and cord blood levels for vitamins A and E for the subjects whose dietary intakes fell below the recommended intake values. In a well-nourished population, it may be possible that other factors such as the mechanisms of placental transfer have a greater influence than maternal diet for maintaining cord levels of these vitamins. Placental transfer of vitamin A has been discussed in other studies (Dancis *et al.* 1992; Sivaprasadarao & Findlay, 1998). Vitamin E is lipid-soluble and is circulated in the blood bound to lipoproteins (Combs, 1998). Lipoprotein receptors in the human placenta have been identified (Wittmaack *et al.* 1995) and the mechanisms for transporting vitamin E to the fetal side of the placenta have been described by Gordon *et al.* (1996). The low level of vitamin E in cord plasma may be due to the fact that the placenta is only slightly permeable to lipid-soluble vitamins (Bohles, 1997) and may also be due to low levels of fetal circulating lipoproteins (Haga *et al.* 1982).

In summary, we found that in a healthy UK obstetric population, maternal dietary intakes were associated with maternal and cord blood levels of β-carotene and vitamin C. For vitamins E and A there was a weaker association between maternal intake and maternal blood levels but no associations were found with cord blood levels.

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