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Selenium status and associated factors in a British National Diet and Nutrition Survey: young people aged 4–18 y

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Objective: Assessment of selenium status to provide normative reference values, and investigation of associated socio-demographic factors, in a national sample of British young people aged 4–18 y.
Setting: National Diet and Nutrition Survey — a nationwide cross-sectional sample of young people aged 4–18 y living in mainland Britain in 1997.
Methods: Selenium status was measured, mainly in fasting blood samples, by plasma selenium concentration in 1127 participants, by red blood cell (RBC) selenium concentration in 1112, and by whole-blood glutathione peroxidase (GPx) activity in 658.
Results: No evidence of severe selenium deficiency or toxicity was observed. Plasma selenium concentration was directly correlated with RBC selenium concentration, and both were associated directly, although less strongly, with GPx activity. Plasma and RBC selenium concentrations increased significantly with age, with RBC concentrations significantly higher in older girls than boys. Region of domicile exhibited a significant relationship. Associations also occurred with parental occupational social class, selenium concentrations being higher in more socially advantaged children. Black and Indian children had considerably higher concentrations than Caucasian children. Concentrations, especially of plasma selenium, were significantly lower in children either (or both) of whose parents were smokers, although, unexpectedly, there was no evidence that children who themselves smoked had lower levels.
Conclusions: The observed associations between selenium status indices and age, gender, social class, parental smoking and ethnic group indicate a complex network of biological factors which determine selenium concentrations in blood components, and which thus need to be controlled for when using these indices to assess selenium status in young people.
Sponsorship: The survey was commissioned jointly by the Department of Health and the Ministry of Agriculture, Fisheries and Food, whose responsibility has since been transferred to the Food Standards Agency. Support for the further analysis presented in this paper was provided by the Department of Health.
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Introduction

Selenium (Se) is an essential dietary trace element for man and for a wide range of animal species. It forms a vital part of the structure of certain proteins, in which Se replaces sulphur in the sulphur-containing amino acids methionine and cysteine, forming selenomethionine and selenocysteine respectively (Combs, 2001). Se is also essential for the activity of key peroxidase enzymes, which exhibit antioxidant activity. Since the measurement of Se in blood compartments and other sites relevant for status assessment requires special equipment, expertise and precautions during collection, and because there is a lack of consensus about the relative value of different Se status indices, there is a need for

more information about Se status in representative population samples (Arthur, 1999; Brown *et al*, 2000; Nève, 2000).

Like most essential trace elements, Se can become toxic at high intakes, especially if prolonged. In places where Se levels are very high, animals and plants may accumulate excessive amounts, thus posing a danger of toxicity to humans (van Vleet & Ferrans, 1992; Xia *et al*, 1992). Conversely, Se deficiency is also a well-established problem for farm animals and human populations in certain parts of the world, and is associated with pathological lesions and with undesirably low biochemical status values (Oldfield, 1999). In the UK, it is uncertain whether the current dietary supply of Se is adequate for optimal human health, to what extent it has changed following recent changes in the origin of wheat flour imports, and whether there may be deleterious results of these changes (MAFF, 1997; Rayman, 2000).

Se status has been measured by a variety of biochemical indicators, with none universally preferred (Nève, 2000). Most surveys of human populations have measured either plasma, serum or red blood cell (RBC) Se concentration, the latter being considered a longer term indicator in relation to variations in dietary Se intake. Another favoured index is the activity of glutathione peroxidase (GPx), a selenoenzyme which can be measured either in blood cells or plasma. It has the potential to reflect functional Se adequacy, reaching a plateau at moderate Se intakes (Whanger, 1998; Arthur, 1999; Nève, 2000).

The purpose of the present study is to summarise newly available data describing the biochemical Se status of a nationally representative sample of British young people (children and adolescents) who participated in the 1997 National Diet and Nutrition Survey of young people aged 4–18 y.

Materials and methods

Survey fieldwork

The survey plan and procedures have been described in detail elsewhere (Gregory *et al*, 2000); therefore only a brief summary is given here. The cross-sectional population sample was obtained from 132 randomly-selected postcode sectors, which were randomly allocated to four sequential 3 month 'rounds' of fieldwork, corresponding approximately to the four seasons, and beginning in January 1997. Participation in each element of the survey was voluntary; therefore not all of the participants complied with all of the elements of the survey. Demographic socio-economic and other information was obtained by questionnaire by a trained interviewer in the participant's home. A weighed dietary record was kept for 7 days, and an early morning, usually fasting, blood sample was taken by a trained phlebotomist. This sample was subdivided and used for the measurement of a wide range of biochemical status analyses in three laboratories. Two of these received samples by first class post, while the third received frozen samples by courier delivery following initial subdivision and freezing in hospital laboratories near the site of collection. Permission was given for the survey procedures by individual Local Research Ethics Committees representing each of the 132 postcode sectors, and by the MRC Dunn Nutrition Unit's Ethics Committee.

Selenium status analyses

The Survey Report (Gregory *et al*, 2000) provides summary results for plasma Se concentration and GPx activity, but not RBC Se concentration. These latter results were measured in a separate commission by the Department of Health. Plasma and RBC Se concentrations were measured in EDTA-stabilised blood samples sent by first class post to the SAS Trace Element Unit at Southampton General Hospital. Each blood sample was immediately centrifuged to separate the plasma, which was removed. The RBC pellet was then reconstituted with saline, and Se concentrations in both fractions measured by inductively coupled plasma mass spectrometry (ICP-MS) (Delves & Sieniawska, 1997). Samples (0.2 ml) of plasma and resuspended RBCs were diluted with 15 vol of a diluent containing 1% v/v butan-1-ol, 0.66% v/v Triton X-100, 0.01 mol/l ammonia, 0.2 mmol/l ammoniumdihydrogen-EDTA and 2 mmol/l ammoniumdihydrogen phosphate (Sieniawska *et al*, 1999). This diluent destabilises argon adducts which would otherwise interfere, and permits accurate analysis of ^{78}Se, the second major natural isotope (23.8% abundance). Matrix-matched standards containing bovine serum were used for calibration. Internal quality assurance sera were prepared by adding Se to bovine sera at 0, 0.4 and 1.6 μmol/l. A Nycomed Seronorm quality control with an assigned value was also used, as a check of accuracy. Participation in external quality assessment schemes organised by the Centre du Toxicologie de Quebec and by the UK TEQAS (Trace Element Quality Assurance Scheme, University of Surrey) provided inter-laboratory comparison. The mean coefficient of variation of five different internal quality controls (which were included with every 10 duplicate test samples) was 5.3%, and the extent of assay drift over the 3 months required to analyse all the samples was less than 1.3%.

In addition to the direct measures of Se status, during survey rounds three and four only, Se status was also assessed indirectly by measuring whole-blood GPx activity (Belsten & Wright, 1995), based on the method of Paglia and Valentine (1967). The whole-blood samples used for the GPx assay were collected in lithium heparin anticoagulant, taken inside a coolbox to a local hospital laboratory (within a maximum of 5 h), and kept frozen for a few weeks at -40°C and then at -80°C before analysis of the enzyme activity at MRC Human Nutrition Research. As a precaution against possible damage, these samples were thawed only once, just before the assay of GPx activity. For quality assurance, bulk heparinised human blood was subdivided and frozen in small aliquots, a single aliquot being thawed for each subsequent assay run, to check for any possible drift or changes in assay sensitivity.

Statistical methods

Statistical analyses were performed using SPSS (SPSS Inc., USA), and included analysis of variance (ANOVA), univariate and multivariate regression. In the Survey Report (Gregory *et al*, 2000), weighting factor adjustments were used to adjust for known socio-demographic differences between the composition of the survey sample and that of the entire (census) population of Great Britain. However, when applied to the Se status indices, these weighting factors made essentially no difference to the results, and have consequently not been used to adjust the results in the present study. $P < 0.05$ indicated statistically significant differences.

Results

Tables 1–3 show summary statistics for plasma and RBC Se concentrations, and GPx activities, by gender and age group. Plasma and RBC Se concentrations increased progressively with age in both sexes (Tables 1 and 2). The magnitude of this change, between 4 and 18 y, was greater in girls than in boys. For GPx activity, there was little evidence of an age trend for boys, although girls exhibited a slight upward trend (Table 3). Gender differences in plasma Se concentration were small and inconsistent in all four age groups (Table 1). For RBC Se concentration, however, although the gender difference was very small in the youngest children, it became

Table 1 Plasma selenium concentration by gender and age group

		Plasma selenium concentration (μmol/l)					
Gender and age group	n	*Mean*	*s.d.*	*Median*	*Geometric mean*	*2.5 percentile*	*97.5 percentile*
Boys							
4–6 y	79	0.83	0.15	0.81	0.82	0.60	1.21
7–10 y	176	0.87	0.15	0.86	0.86	0.58	1.19
11–14 y	176	0.84	0.14	0.84	0.83	0.60	1.14
15–18 y	159	0.89	0.14	0.89	0.88	0.64	1.20
All boys	590	0.86	0.15	0.85	0.85	0.61	1.17
Girls							
4–6 y	76	0.82	0.15	0.83	0.80	0.45	1.15
7–10 y	133	0.90	0.16	0.88	0.88	0.61	1.37
11–14 y	165	0.85	0.14	0.83	0.84	0.63	1.16
15–18 y	163	0.91	0.14	0.91	0.90	0.63	1.21
All girls	537	0.88	0.15	0.86	0.86	0.60	1.22
All boys and girls	1127	0.87	0.15	0.86	0.86	0.61	1.20

Significance of univariate linear regressions between plasma selenium and age was: boys — $t = 2.1$, $P = 0.03$, 558 d.f.; girls — $t = 4.2$, $P < 0.001$, 535 d.f. None of the individual age groups' values differed significantly between the genders, $P \geq 0.05$ for all four age groups.

Table 2 Red cell selenium concentration by gender and age group

		Red cell selenium concentration (μmol/l)					
Gender and age group	n	*Mean*	*s.d.*	*Median*	*Geometric mean*	*2.5 percentile*	*97.5 percentile*
Boys							
4–6 y	77	1.41	0.27	1.36	1.39	1.01	2.06
7–10 y	174	1.44	0.26	1.41	1.41	1.04	2.04
11–14 y	174	1.44	0.28	1.40	1.42	1.06	2.12
15–18 y	156	1.46	0.25	1.44	1.44	1.03	1.97
All boys	581	1.44	0.26	1.41	1.42	1.03	2.03
Girls							
4–6 y	74	1.46	0.30	1.42	1.43	0.96	2.28
7–10 y	132	1.56	0.35	1.53	1.53	0.97	2.67
11–14 y	162	1.57	0.31	1.53	1.54	1.13	2.46
15–18 y	163	1.67	0.32	1.68	1.64	1.10	2.25
All girls	531	1.58	0.33	1.54	1.55	1.06	2.44
All boys and girls	1112	1.51	0.30	1.47	1.48	1.05	2.22

Significance of univariate linear regressions between red cell selenium and age was: boys — $t = 1.2$, $P = 0.23$, 579 d.f.; girls — $t = 5.4$, $P < 0.001$, 529 d.f. Gender differences within the four age groups were: 4–6 y — $t = 1.1$, $P = 0.29$, 149 d.f.; 7–10 y — $t = 3.7$, $P < 0.001$, 304 d.f.; 11–14 y — $t = 3.8$, $P < 0.001$, 334 d.f.; 15–18 y — $t = 6.7$, $P < 0.001$, 317 d.f.

Table 3 Blood glutathione peroxidase activity by gender and age group

		Blood glutathione peroxidase activity (nmol/mg Hb/min)					
Gender and age group	n	*Mean*	*s.d.*	*Median*	*Geometric mean*	*2.5 percentile*	*97.5 percentile*
Boys							
4–6 y	42	91.0	18.6	90.0	89.4	69.0	169.7
7–10 y	106	88.3	17.1	86.0	86.7	61.7	135.0
11–14 y	102	88.8	14.7	88.5	87.6	63.6	123.0
15–18 y	87	92.8	24.0	89.0	90.5	61.4	166.4
All boys	337	90.0	18.7	88.0	88.3	63.4	131.8
Girls							
4–6 y	47	90.1	18.8	85.0	88.4	60.2	155.0
7–10 y	83	90.7	18.0	88.0	89.2	66.0	148.9
11–14 y	93	98.1	20.3	97.0	96.2	64.0	147.0
15–18 y	98	93.0	18.8	91.5	91.3	68.0	141.5
All girls	321	93.5	19.2	90.0	91.7	66.0	143.0
All boys and girls	658	91.7	19.0	89.0	89.9	65.0	141.0

Significance of univariate linear regressions between glutathione peroxidase and age were not significant ($P \geq 0.05$). Differences between the genders for individual age groups were not significant, with the exception of the 11–14 y group, where $t = 3.7$, $P < 0.001$, 193 d.f.

progressively larger as the children became older, with much higher concentrations in older girls (Table 2). For GPx activity, gender differences were small and inconsistent (Table 3).

Table 4 investigates relationships between the three Se status indices. In order to minimise the possibility of confounding by age and gender covariance, analyses were carried out for each age and gender group separately. From Table 4, strong direct linear relationships were found between plasma Se and RBC Se concentrations, for all eight age–gender subgroups, thus confirming that plasma and RBC Se concentrations are strongly inter-related. However, the relationship between plasma Se concentration and GPx activity, although generally positive, was much weaker, and achieved statistical significance in only three of the eight age–gender subgroups. The relationship between RBC Se concentration and GPx activity was also weak; indeed none of the eight age–gender subgroup comparisons exhibited a significant direct relationship. Thus, there is no evidence that activity of GPx (which is principally an RBC enzyme) is more strongly related to the concentration of Se in RBCs than in plasma. There is no convincing evidence of a plateau in GPx activity at the higher concentrations of Se in either plasma or RBCs.

Table 5 shows significant evidence of regional variation in both plasma and RBC Se concentrations, whereas this was not found with GPx activity. The patterns of regional variation for plasma and RBC Se concentrations were consistent

Table 4 Regression analyses with plasma selenium and glutathione peroxidase as the dependent variables

	Plasma selenium as dependent variable			*Glutathione peroxidase as dependent variable*					
	Red cell selenium			*Plasma selenium*			*Red cell selenium*		
Gender and age group	*d.f.*	t	P	*d.f.*	t	P	*d.f.*	t	*P*
Boys									
4–6 y	74	4.1	< 0.001	38	3.1	0.004	38	2.0	0.05
7–10 y	171	8.7	< 0.001	102	0.7	0.50	102	1.3	0.20
11–14 y	171	8.0	< 0.001	97	− 0.8	0.45	97	1.0	0.33
15–18 y	153	8.7	< 0.001	83	2.4	0.02	83	1.0	0.30
All boys	578	14.6	< 0.001	329	2.5	0.012	329	2.6	0.009
Girls									
4–6 y	71	6.4	< 0.001	41	0.04	0.97	41	0.2	0.81
7–10 y	129	8.0	< 0.001	79	0.3	0.75	78	0.9	0.38
11–14 y	159	7.3	< 0.001	90	− 0.3	0.80	89	0.9	0.37
15–18 y	160	8.1	< 0.001	93	3.1	0.003	93	1.6	0.11
All girls	528	15.4	< 0.001	312	1.1	0.29	310	1.5	0.13
All boys and girls	1109	21.1	< 0.001	644	2.7	0.007	642	3.4	< 0.001

All regressions adjusted for age.

Table 5 Selenium status indices by region

	Plasma selenium (μmol/l)		*Red cell selenium (μmol/l)*		*Glutathione peroxidase (nmol/mg Hb/min)*	
Region	n	*Mean*	n	*Mean*	n	*Mean*
Scotland	78	0.83	75	1.46	52	92.1
Northern England	287	0.89	283	1.52	166	92.1
Central and south-west England, and Wales	409	0.84	407	1.44	246	89.3
London and south-east England	353	0.89	347	1.59	194	94.2
Inter-class *F*-ratio		8.3		15.7		2.4
P		<0.001		<0.001		0.07

ANOVA models adjusted for age and gender.

between the two indices, but did not reveal a simple (eg north–south) gradient. The highest concentrations were observed in the northern England and in London and the south-east, while the lowest concentrations occurred in Scotland and in the central, south-west and Welsh regions.

Table 6 shows significant evidence of a relationship between Se status and occupational social class of head of household, with highest mean concentrations of plasma Se being associated with classes I and II. This relationship was only significant for plasma Se concentration; being absent for RBC Se concentration and GPx activity, respectively. If either household income or highest maternal educational qualifications were substituted for occupational social class of head of household, the picture was similar, there being a highly significant direct correlation with plasma Se concentration but no significant correlation with RBC Se concentration or with GPx activity. If receipt (*vs* no receipt) of state income supplements (family credit or income support) was substituted as the measure of financial adequacy, no significant relationship with any of the three Se indices was detectable.

Table 7 shows that, although 95% of children in the survey were of Caucasian origin, there was a marked and highly significant difference between different ethnic

Table 6 Selenium status indices by occupational social class of head of household

	Plasma selenium (μmol/l)		*Red cell selenium (μmol/l)*		*Glutathione peroxidase (nmol/mg Hb/min)*	
Occupational social class	n	*Mean*	n	*Mean*	n	*Mean*
I and II (professional, managerial and technical)	381	0.88	378	1.52	227	90.7
IIInm (skilled non-manual)	142	0.86	140	1.47	96	91.5
IIIm, IV and V (skilled manual and unskilled)	510	0.85	502	1.50	312	92.0
Inter-class *F*-ratio		5.2		2.4		0.2
P		0.006		0.09		0.81

ANOVA models adjusted for age and gender.

Table 7 Selenium status indices by ethnic group

	Plasma selenium (μmol/l)		*Red cell selenium (μmol/l)*		*Glutathione peroxidase (nmol/mg Hb/min)*	
Ethnic group	n	*Mean*	n	*Mean*	n	*Mean*
Caucasian	1026	0.86	1013	1.48	602	91.7
Black (Afro-Caribbean)	26	0.91	26	1.88	15	98.3
Indian sub-continent	50	0.96	49	1.79	25	85.8
Others and mixed race	25	0.90	24	1.65	16	93.1
Inter-class *F*-ratio		8.4		28.0		1.4
P		<0.001		<0.001		0.25

ANOVA models adjusted for age and gender.

groups, for both plasma and RBC Se concentration, but not GPx activity. Children who were black or from the Indian sub-continent had higher concentrations of Se in plasma and RBCs than those of Caucasian origin. Inter-group differences were especially large, and highly significant, for RBC Se concentration. Inclusion of region (four subdivisions) in the ANOVA model did not alter the significance of the ethnic group differences in the selenium indices, therefore these differences do not appear to be an artefact of covariant regional differences.

Table 8 shows that, after adjustment for age and gender, none of the three Se status indices differed between children who were smokers and those who reported being non-smokers. This conclusion remained true whether all children were included, or whether only the 15–18-y-old age group was examined, where nearly all the smokers occurred. However, an analysis of parental smoking gave a contrasting result: children whose mothers or fathers (or both) were smokers had significantly lower plasma and RBC Se concentrations than those whose parents were non-smokers. This was strongest for plasma Se concentration and maternal smoking, with findings not confined to a particular age group. If social class indicators (Registrar General classification of head of household, family income, receipt of family credit or income support and maternal educational qualifications) were included in the model, there was a moderate reduction in the significance of the parental smoking index, but it still remained as a highly significant covariate, with both plasma and RBC Se concentration.

There were no significant associations between any of the Se status indices and the anthropometric indices measured (weight, height, mid upper-arm circumference, waist and hip circumferences — not shown). Neither menarcheal status (in 12–13-y-old girls) nor self-reported use of contraceptive pills (in 16–18-y-old girls) was significantly related to any of the Se indices measured here. Likewise, there were no associations between Se status and either systolic blood pressure or pulse rate (not shown). However, a direct relationship did exist between both plasma and RBC Se concentrations and diastolic blood pressure ($P=0.001$ and $P=0.02$ for plasma and RBC Se concentrations, respectively). This relationship was stronger in girls than boys (not shown).

When subdivided by season of blood collection, and analysed with adjustments for age and gender, there was

Table 8 Selenium status indices by smoking habit of young person or their parents

	Plasma selenium (μmol/l)		*Red cell selenium (μmol/l)*		*Glutathione peroxidase (nmol/mg Hb/min)*	
Cigarette smoking category	n	*Mean*	n	*Mean*	n	*Mean*
Smoking category of young person (all respondents[a])						
Smoker	122	0.89	122	1.53	81	93.2
Non-smoker	823	0.87	814	1.52	473	91.6
Inter-class *F*-ratio		0.02		2.6		0.0
P		0.88		0.10		0.99
Maternal smoking category (all respondents[b])						
Smoker	346	0.84	340	1.46	199	92.2
Non-smoker	737	0.88	729	1.53	428	91.2
Inter-class *F*-ratio		23.6		14.5		0.5
P		<0.001		<0.001		0.48
Paternal smoking category (all respondents[c])						
Smoker	272	0.84	269	1.47	162	91.0
Non-smoker	639	0.88	630	1.52	370	92.4
Inter-class *F*-ratio		16.9		3.6		0.5
P		<0.001		0.06		0.49
Both parents smoking (all respondents[c])						
Both smoking	149	0.83	147	1.43	90	93.2
Neither smoking	520	0.89	514	1.52	305	92.5
Inter-class *F*-ratio		19.7		10.0		0.2
P		<0.001		0.002		0.65

ANOVA models adjusted for age and gender.
[a]Remaining non-significant ($P \geq 0.05$) if confined to the 15–18-y-old age group, which contains 113 of the 139 smokers in the survey.
[b]When the four age groups were tested separately, there was a significant ($P < 0.05$) relationship with maternal smoking habit for the 4–6 y, 7–10 y and 15–18 y age groups for plasma selenium concentration, and for the 4–6 y and 11–14 y age groups for red cell selenium concentration.
[c]When the four age groups were tested separately, there was a significant ($P < 0.05$) relationship with paternal smoking habit for the 4–6 and 15–18 y age groups for plasma selenium concentration, but not for any of the individual age groups for red cell selenium concentration.

some evidence of seasonal variation, with higher values in the winter and spring months and lower values in the summer and autumn months, for both plasma and RBC Se concentration, the level of significance being higher for plasma than for RBC Se (not shown). Blood GPx measurements spanned only half of the year.

Plasma Se concentration, and to a lesser extent both RBC Se concentration and GPx activity, were significantly (and generally positively) correlated with several other biochemical indices measured in the survey (Gregory *et al*, 2000), after correction for age and gender covariance. Using a significance level of $P < 0.01$, of the 52 individual comparisons tested for each Se status index, 19 were significant for plasma Se concentration, nine for RBC Se concentration, and nine for GPx activity (not shown). The only significant inverse associations encountered were between plasma concentrations of Se and alkaline phosphatase, RBC Se and plasma 25-hydroxyvitamin D concentrations, and between GPx activity and plasma total (and low density lipoprotein) cholesterol concentration. The inverse association between RBC Se and plasma 25-hydroxyvitamin D concentrations was reduced but not eliminated by including season of blood collection in the model, suggesting some seasonal covariance. All other significant associations were direct, encompassing many of the plasma indices measured for minerals, fat- and water-soluble vitamins, and for clinical chemistry assessment such as plasma cholesterol and urea. The patterns of association did not, however, suggest any simple underlying mechanism. Neither plasma nor RBC Se concentration was significantly related to plasma α_1-antichymotrypsin concentration (the biochemical marker used to test for abnormal acute-phase status), whereas a direct association was found with GPx activity ($P < 0.001$).

Discussion

Compared with biochemical Se status concentrations reported previously in the UK (Lloyd *et al*, 1989; Thomas *et al*, 1994) and from other countries in Europe and elsewhere (van Caillie-Bertrand *et al*, 1986; Chakar *et al*, 1993; Malvy *et al*, 1993; Mussalo-Rauhamaa *et al*, 1993; Rossipal & Tiran, 1995; Cser *et al*, 1996; Mengubas *et al*, 1996; Micetic-Turk *et al*, 1996; Rükgauer *et al*, 1997; Wang *et al*, 1998; Brtkova *et al*, 1999), those of the present survey (Tables 1 – 3) lie near the middle. It has been known for many years that both high and low extremes of Se status are encountered in parts of China (Oldfield, 1999; Combs, 2001), with high concentrations also found in parts of the mid-west USA due to extremes of soil Se content (Oldfield, 1999). A quarter of a century ago, there were low levels reported from Finland and New Zealand because of low soil Se contents. However, both of these countries have reported improvements in Se status in the last two decades, due either to the use of Se-enriched fertilisers (in Finland, Wang *et al*, 1995, 1998), or the importation of grain from countries such as Australia, with a higher soil Se content (for New Zealand, Watkinson, 1981; Thomson & Robinson, 1996). It is likely that those of Britain are still declining (Rayman, 2000).

Virtually all studies on children of different ages have provided evidence of progressively increasing Se concentrations (in plasma and blood) with increasing age (van Caillie-Bertrand *et al*, 1986; Malvy *et al*, 1993; Mussalo-Rauhamaa *et al*, 1993; Thomas *et al*, 1994; Rossipal & Tiran, 1995; Cser *et al*, 1996; Micetic-Turk *et al*, 1996; Bartkova *et al*, 1999). It occurs most rapidly in very young children, and continues throughout childhood and adolescence. This appears to be a normal physiological trend, presumably associated with tissue maturation. The present study has confirmed this maturational pattern (Tables 1 and 2), and has provided new evidence of significant gender differences, specifically in RBC Se concentration, which appear not to have been reported before.

Some previous studies of Se status in children have noted the existence of direct correlations between blood Se concentrations and GPx activities, between individuals (van Caillie-Bertrand *et al*, 1986; Lloyd *et al*, 1989; Cser *et al*, 1996), although this is not a universal observation (Chakar *et al*, 1993). In the present study, the relationships between plasma concentrations of Se or RBC Se and GPx activity were relatively weak, even though the two concentration indices were very strongly correlated with each other (Table 4). This result would be expected if the Se supply was sufficient to ensure near-saturation of the requirements for maximal GPx activity, such that its variance was relatively insensitive to moderate variations in the Se supply. However, the observed shapes of the associations between GPx activity and plasma or RBC Se concentrations in the present study, with no sign of a plateau, do not appear to support this explanation. More evidence about the adequacy of Se intakes in Britain is needed on the basis of Se intake data. Studies to address the need for an up-to-date British food-Se database are ongoing. The evidence for regional variations in Se status indices (Table 5) is intriguing and deserves further investigation to determine whether it might be attributable to differences in natural soil Se levels, in the use of Se-containing fertilisers, or whether local variations in traditional food choices could be relevant.

As noted in the Survey Report (Gregory *et al*, 2000), micronutrient status index values are frequently correlated with indices of family socio-economic status and wealth; higher values often being encountered in the more advantaged families. Plasma Se concentration in particular follows this pattern (Table 6), and the possible link with diet quality needs to be tested in the light of Se intake estimates. To the authors' knowledge there is little published information about socio-economic determinants of Se status. Likewise, apart from recent evidence of higher plasma Se concentration and RBC GPx activity in a small number of African-American children compared with their Caucasian counterparts (Glauser *et al*, 1999), ethnic differences in Se status indices appear not to have been reported elsewhere (Alfthan & Nève, 1996). It seems unlikely that the non-Caucasians,

who had higher plasma and RBC Se concentrations (Table 7), also had higher Se intake than the Caucasians. Therefore, a more probable explanation is that there are biological differences in the control of absorption or distribution of Se between ethnic groups, which manifest as differences in blood Se concentrations. It will be of considerable interest to ascertain whether these differences persist into adulthood, and whether there are any functional consequences.

The relationships between Se status and smoking habit (Table 8) were unexpected. Despite no evidence of any status differences between children who were themselves smokers and those who reported that they were not, there were highly significant differences, at all ages, according to parental smoking habit and especially maternal smoking. While an effect of passive smoking cannot be ruled out, this appears to be an improbable explanation, and other associated lifestyle factors, possibly associated with social class, need to be considered. An effect of smoking habit on Se status indices has been documented previously in only one of four studies (Alfthan & Nève, 1996).

The absence of a significant correlation between plasma Se and the acute-phase index, α_1-antichymotrypsin, despite published evidence that Se is a negative acute-phase reactant (Galloway *et al*, 2000) suggests that acute phase effects are usually of minimal importance in this age group. It is also of interest that, despite the observed gender difference in RBC Se concentrations, oral contraceptive users had RBC Se concentrations that did not differ significantly from those of non-users.

The correlation between Se concentrations and diastolic blood pressure is intriguing, but cannot be explained satisfactorily at present. The evidence of possible seasonal variation in plasma and RBC Se concentrations should be viewed with caution, since it was difficult, in view of the survey constraints, to eliminate the possibility of analytical artefact with complete certainty. This observation therefore requires confirmation, but suggests an interesting avenue for future investigation. Likewise, although it is difficult to explain the origin of the wide-ranging correlations seen between the Se indices and other biochemical status index values in blood, these may help to reveal metabolic and nutritional associations with potential functional significance. Some of these correlations may represent the covariance of certain nutrients in foods and diets, thus reflecting persistent differences in dietary choices between individuals. Others may reflect covariant physiological changes during tissue maturation, which cannot be fully corrected for, by inclusion of age as a covariate in the statistical models. Some may represent genetically driven covariance of homeostatic control mechanisms involving blood nutrient levels. We are faced with an important challenge, to try to identify those indices which are susceptible to modulation by intervention, and which are also of relevance to the prediction or control of preventable disease processes.

This is the first nationwide study of Se status in a representative sample of British children aged 4–18 y, which provides a normative set of reference values for comparison with future studies, including those investigating special population or patient groups.

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