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Serum selenium determinants in French adults: the SU.VI.M.AX study

J. Arnaud[1,2]*, S. Bertrais[3], A. M. Roussel[2], N. Arnault[3], D. Ruffieux[1], A. Favier[1], S. Berthelin[1], C. Estaquio[3], P. Galan[3], S. Czernichow[3] and S. Hercberg[3]

[1]*Département de Biologie Intégrée, CHU de Grenoble, BP 217, 38043 Grenoble cedex 9, France*
[2]*Nutrition, Vieillissement et Maladies Cardiovasculaires, Faculté de Pharmacie, Université Joseph Fourier, Domaine de la Merci, 38700 La Tronche, France*
[3]*U557 Inserm (UMR Inserm-Inra-Cnam), Institut Scientifique et Technique de la Nutrition et de l'Alimentation, 5 rue Vertbois, 75003 Paris, France*

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The objective of the present work was to assess the relationship between serum Se concentrations and environmental determinants (i.e. lifestyle, social activity, geographic region, urban status, education, familial status, physical activity, BMI, tobacco, and food and alcohol consumption). Baseline results from 13 017 subjects (7876 women aged 35–60 and 5141 men aged 45–60) who participated in the SU.VI.M.AX (Supplémentation en Vitamines et Minéraux Antioxydants) study were analysed. Fewer than 2 % of the volunteers had a serum Se status under 0·75 μmol/l, which has been quoted as the cut-off of biological Se sub-deficiency. Women had significantly lower serum Se concentrations than men (1·09 (SD 0·19) μmol/l (*n* 7423) and 1·14 (SD 0·20) μmol/l (*n* 4915), $P<0·0001$, respectively). Significant differences in serum Se concentrations were observed between geographic areas. In both sexes, the serum Se concentration increased with alcohol, meat and fish consumption, and decreased with smoking. In premenopausal women, the serum Se concentration was higher in contraceptive-pill users than in non-users. In women only, age was associated with increased serum Se concentrations, and obesity (BMI $\geq 30\,kg/m^2$) was associated with decreased serum Se levels. In men, we observed a decrease in serum Se concentrations with increased consumption of vegetables and fruits. In conclusion, though few of the volunteers participating in the SU.VI.M.AX study had Se status in the sub-deficiency range, 83 % of women and 75 % of men had serum concentrations below the value considered optimal for glutathione peroxidase activity. The largest Se associations in both sexes were found with regions, smoking, alcohol, meat and fish consumption. Further studies are needed to understand the difference in Se status between genders.

Selenium in serum: Selenium determinants: Human nutrition: Lifestyle

The SU.VI.M.AX (Supplémentation en Vitamines et Minéraux Antioxydants) study was a French large-scale longitudinal intervention trial performed in order to evaluate the efficacy of a daily combination of micronutrient antioxidants (vitamins C and E, β-carotene, Zn and Se), at non-pharmacological doses, in reducing the incidence of cancers and cardiovascular diseases. After 7·5 years of follow-up, results from this randomized, double-blind, placebo-controlled, primary-prevention trial showed that combined antioxidant supplementation decreased the risk of cancer in men, and this protective effect was greater among those with low baseline concentrations of serum vitamin C or vitamin E (Hercberg *et al.* 2004). This stimulated interest in identifying factors able to modulate the level of blood antioxidant markers.

Serum Se is considered to be a good index of Se status (Nève, 1991), though previous investigations of determinants of Se status yielded conflicting results (Robberecht & Deelstra, 1994; Alfthan & Nève, 1996). The present cross-sectional study focused on socio-demographic, lifestyle and dietary factors related to serum Se concentrations in participants in the SU.VI.M.AX study at baseline.

Materials and methods

Subjects

The design of the SU.VI.M.AX study and the characteristics of the participants at baseline have been previously described (Hercberg *et al.* 1998, 2004). Briefly, 13 017 subjects (5141 men aged 40–60 years and 7876 women aged 35–60 years) were recruited between October 1994 and May 1995 with a planned follow-up of 8 years. These subjects were recruited after a 5-month national multimedia campaign (March to July 1994). At enrolment, all participants supplied details of their past medical history as well as anthropometric, demographic and lifestyle data, and declared themselves to be free of any severe pathologies. Baseline characteristics showed that this cohort was close to the national population in terms of geographic density and socio-economic status (Hercberg *et al.* 1998).

Abbreviation: SU.VI.M.AX, Supplémentation en Vitamines et Minéraux Antioxydants.

* **Corresponding author:** Dr J. Arnaud, fax +33 4 76 76 58 21, email JArnaud@chu-grenoble.fr

All subjects gave their informed written consent to the study. The protocol was approved by a medical ethics committee (CCPPRB no. 706 Paris-Cochin Hospital, France) and the national committee for the protection of privacy and civil liberties (CNIL no. 334641).

Socio-demographic and lifestyle data

Socio-demographic and lifestyle data were obtained from a questionnaire at baseline. Six categories of age were defined: <40 years, 40 to <45 years, 45 to <50 years, 50 to <55 years, 55 to <60 years and ≥ 60 years, with the first one including only women. Family status was categorized as one of two categories (couple life or not). Educational level was coded as three categories according to the highest degree obtained (primary school, high school, university or equivalent). Occupation was separated into three categories (workers, unemployed and retired). France was divided into eleven geographic regions (Alps, Brittany, Burgundy, Centre, Loire lands, Mediterranean coast, Normandy, North, Northeast, Paris outskirts, Southwest). The place of residence was defined by the zip code of each subject at baseline. Four categories were defined according to the definition of the Institut National de la Statistique et des Etudes Economiques (I.N.S.E.E., Paris, France) based on the economic activity of the area corresponding to each subject's zip code (Le Jeannic & Vidalenc, 1997): urban municipalities provided at least 5000 jobs; suburbs were defined as municipalities surrounding an urban pole; mixed municipalities were those located outside an urban area, but where at least 40 % of the resident population worked in an urban area; and rural municipalities consisted of all other zip codes or municipalities. Five categories of smoking habits were defined: never smokers, former smokers, light current smokers if less than ten cigarettes per day, heavy current smokers if more than twenty cigarettes per day and moderate current smokers if the number of cigarettes smoked per day varied from ten to twenty. Alcohol consumption was divided into three categories: non-drinkers, moderate and heavy drinkers. The cut-off between these two groups was defined at 15 g/d for women and 20 g/d for men, taking into account the gender differences in alcohol metabolism and in alcohol consumption associated with increased medical risk (Bradley *et al.* 1998; de Lorimier, 2000; Hines & Rimm, 2001). Among the drinkers, two categories were defined taking into account red wine consumption (yes or no). BMI was divided into three categories ($<25\,kg/m^2$, $25- <30\,kg/m^2$, $\geq 30\,kg/m^2$). Physical activity was also divided into three categories (irregular physical activity; <1 h of walking per day, ≥ 1 h of walking per day). Menopausal status was assessed by a specific questionnaire. In premenopausal women, four categories of contraceptive use were defined (no contraceptive method, contraceptive-pills, intrauterine device, other contraceptive methods). In postmenopausal women, two categories were defined based on current use of hormone replacement therapy (yes or no).

Dietary assessment

Data on dietary intake were available for a subsample of 6390 subjects who agreed to report at least six 24 h dietary records during the first 2 years of the study. The record days (two weekend days and four week days) were randomly assigned to volunteers and covered all seasons. These subjects had serum Se concentrations (1·13 (SD 0·20) μmol/l, *n* 2717 men; 1·09 (SD 0·18) μmol/l, *n* 3673 women) similar to those of the participants who did not agree to fill out dietary questionnaires (1·14 (SD 0·20) μmol/l, *n* 2199 men, $P=0{\cdot}40$; 1·09 (SD 0·20) μmol/l, *n* 3752 women, $P=0{\cdot}62$) during the first 2 years of the study. For the collection of dietary data, volunteers received a free small terminal specifically developed for the study and loaded with *ad hoc* software. This material enabled subjects to fill out computerized questionnaires off-line and to transmit data during a brief telephone connection via the Minitel Telematic Network, which connected them to the main SU.VI.M.AX computer server. The Minitel is a small terminal which was widely used at the beginning of the SU.VI.M.AX study in France as an adjunct to the telephone. Subjects were assisted in this task by the interactive facilities of the software, and by an instruction manual for coding foods, including photographs for estimations of portion size validated on 780 subjects in a pilot study (Le Moullec *et al.* 1996). Data were also collected on cooking methods, seasoning, type of foods (i.e. fresh, frozen, canned), and place and time of food intake. All dietary values reported here were based on the average intakes for six 24 h dietary records for each subject. For each selected food group, four categories (<25th percentile, $25- <50$th percentile, $50- <75$th percentile, ≥ 75th percentile), were used for the analysis.

Blood analysis

At baseline, venous blood samples from subjects after a 12 h fast were collected in trace-element controlled Vacutainer® tubes (Becton Dickinson, Pont de Claix, France) in 12 338 out of 13 017 participants. Samples were delivered to Grenoble (University Hospital, Grenoble, France) in dry ice and kept frozen until analysed.

Se was determined in serum using electrothermal atomic absorption spectrometry (4100 ZL; Perkin Elmer, Norwalk, CT, USA) according to Arnaud *et al.* (1993). A Se electrodeless discharge lamp and a Zeeman longitudinal background correction were used. The matrix modifier used was Pt. A fivefold-diluted serum in a solution containing 0·1 M-nitric acid and 0·2 % (w/v) Triton X-100 (20 μl) and 30 μg Pt was introduced on to the platform of a pyrolytic graphite furnace. Addition calibration was used and Seronorm® trace element serum was chosen as internal quality control (Sero®, Billingstad, Norway). In addition, the laboratory has participated in two interlaboratory comparison trials organized by the French Society for Clinical Biology (SFBC, Nancy, France) and the Centre de toxicologie du Québec (Sainte-Foy, Québec, Canada) since 1988.

Statistics

Data were processed on an alpha-VMS system, and a specific database was developed using the Statistical Analysis System version 8.2 (SAS Inc., Cary, NC, USA). Serum Se concentrations were compared between men and women by Student's *t* test. The χ^2 test was used when appropriate. Serum Se values were expressed as means and standard deviations or as percentages. Further analyses

were performed in men and women separately. The mean levels of serum Se were compared across categories of age, couple status, educational level, occupation status, geographic region, type of residence location, BMI, physical activity, smoking habits, alcohol and selected food consumption, and hormonal status, using the Fisher's test and/or by a test for a linear trend across categories. $P<0{\cdot}05$ was considered as significant.

Results

Women had a lower mean level of serum Se than men: 1·09 (SD 0·19) μmol/l (*n* 7423) for women and 1·14 (SD 0·20) μmol/l (*n* 4915) for men ($P<0{\cdot}0001$). All other analyses were therefore done separately in men and women. The percentages of serum Se values below 0·75 μmol/l, considered to be a sub-deficient level by a European group of scientists (Van Dael & Deelstra, 1993), were 1·3 % in men and 1·7 % in women. The percentages of serum Se values higher than 1·25 μmol/l, which corresponds to optimal glutathione peroxidase activities (Nève, 2000; Rayman, 1997), were 25·3 % in men and 17·4 % in women. The unadjusted mean levels of serum Se by geographic region are presented separately in men (Fig. 1(A)) and women (Fig. 1(B)). The regional differences remained significant ($P<0{\cdot}0001$) after adjustment for age, smoking habits and education. The highest mean values were found in the North and in Normandy and the lowest in the Centre. With the exception of Brittany, the same geographic differences were observed in men and women. Table 1 presents the relationships between serum Se levels and socio-demographic data. The relationships between serum Se levels and couple status, educational level or occupational status altered with adjustment factors. In men, the type of resident area did not consistently influence serum Se levels although the global significance test was statistically significant. Serum Se concentrations increased with age in women ($P<0{\cdot}0001$), but not in men, whatever the adjustment factors included (Fig. 2).

In addition, premenopausal women had serum Se concentrations lower than postmenopausal women (1·07 (SD 0·19) μmol/l, *n* 5263 *v.* 1·12 (SD 0·20) μmol/l, *n* 2012; $P<0{\cdot}0001$). This difference remained significant after controlling for age, smoking, education and region ($P<0{\cdot}04$) or when the analysis was performed in women aged 40–55 years (unadjusted $P<0{\cdot}0001$ and adjusted $P=0{\cdot}04$). In postmenopausal women, the use of hormonal supplement was not associated with a difference in Se serum concentrations (1·12 (SD 0·20) μmol/l, *n* 1225 *v.* 1·12 (SD 0·20) μmol/l, *n* 787, $P>0{\cdot}86$). However, in premenopausal women, those who used contraceptive-pills had higher serum Se concentrations (1·12 (SD 0·19) μmol/l, *n* 908, $P<0{\cdot}001$) compared to those using an intrauterine device (1·06 (SD 0·18) μmol/l, *n* 1554), another contraceptive method (1·06 (SD 0·18) μmol/l, *n* 617) or no contraceptive method (1·07 (SD 0·19) μmol/l, *n* 2050). These differences remained significant after adjustment for age, smoking habits, education and regions.

As shown in Table 2, obese women (BMI $\geq 30\,kg/m^2$) had significantly lower serum Se concentrations than non-obese women. In both sexes, mean serum Se levels did not differ across physical activity groups. Smoking habits were inversely related to serum Se values, and a positive relationship was observed with alcohol intake. Red wine users had significantly higher serum Se concentration than other alcoholic drink users (1·14 (SD 0·20) μmol/l, *n* 2396 *v.* 1·10 (SD 0·19) μmol/l, *n* 205, $P=0{\cdot}009$, in men; 1·09 (SD 0·18) μmol/l, *n* 2459 *v.* 1·08 (SD 0·19) μmol/l, *n* 731, $P=0{\cdot}03$, in women). This difference remained significant only in men after controlling for age, smoking, education, region and alcohol consumption ($P=0{\cdot}03$ in men and $P=0{\cdot}20$ in women). An increase in

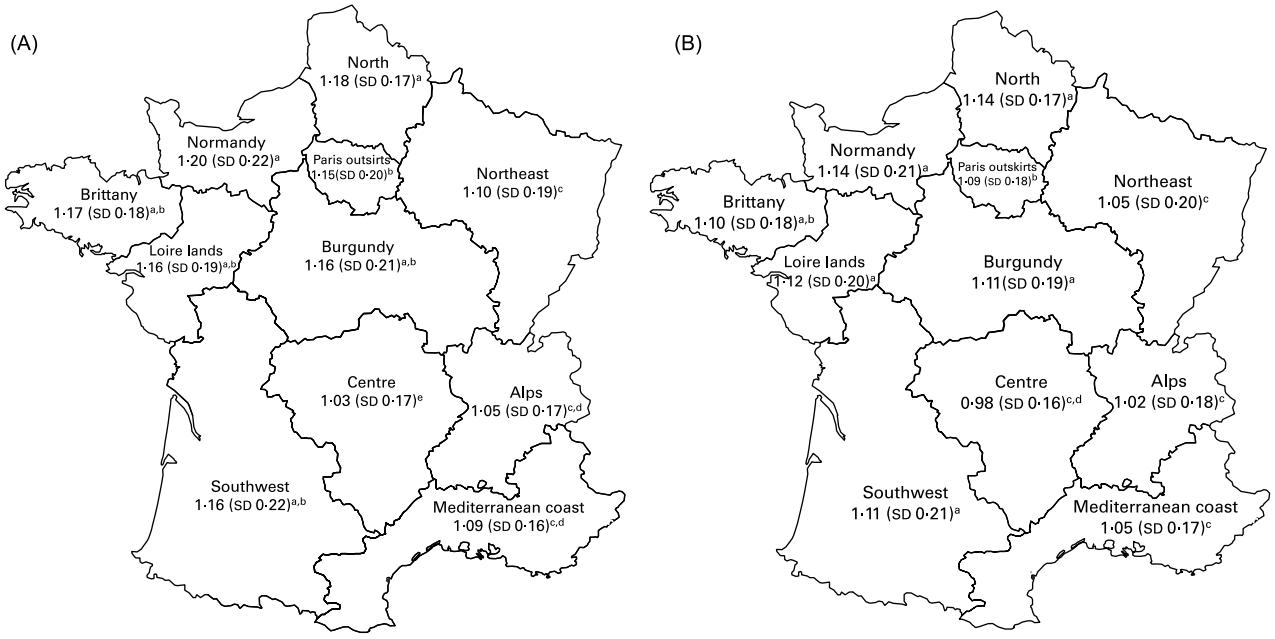

Fig. 1. French map of serum selenium concentrations (μmol/l) in men (A) and women (B). Values are means and standard deviations. [a,b,c,d,e]Mean values with unlike superscript letters were significantly different ($P<0{\cdot}05$). Global adjusted or not $P<0{\cdot}0001$; adjustment for age, smoking habits and education.

Table 1. Relationship between occupation, environment, couple status and education, and unadjusted serum selenium concentrations (μmol/l)
(Mean values and standard deviations)

	Men			Women		
	Mean	SD	*n*	Mean	SD	*n*
Couple status						
No	1·12	0·21	551	1·08	0·19	1577
Yes	1·14	0·20	4244	1·09	0·19	5681
Unadjusted *P*	0·14			0·06		
Adjusted *P**	0·21			0·03		
Education						
Primary school	1·13	0·22	1179	1·10	0·20	1413
High school	1·13	0·20	1733	1·09	0·19	2900
University	1·14	0·19	1944	1·08	0·19	3000
Unadjusted *P* for trend	0·13			0·01		
Adjusted *P* for trend†	0·21			0·49		
Occupation						
Employed	1·14	0·19	3950	1·09[a]	0·19	5555
Unemployed	1·14	0·22	333	1·08[a]	0·19	1451
Retired	1·13	0·21	607	1·11[b]	0·21	365
Global unadjusted *P*	0·43			0·04		
Global adjusted *P**	0·63			0·18		
Resident area						
Urban	1·14[c]	0·20	3243	1·09	0·19	5049
Suburban	1·14[c]	0·19	716	1·08	0·20	1009
Mixed	1·10[c]	0·19	135	1·08	0·19	190
Rural	1·12[c]	0·19	811	1·09	0·19	1158
Global unadjusted *P*	0·02			0·87		
Global adjusted *P*‡	0·04			0·92		

* Adjustment for age, smoking habits, education and region.
† Adjustment for age, smoking habits and region.
‡ Adjustment for age, smoking habits and education.
[a,b,c]Means within the levels of variables with unlike superscript letters were significantly different ($P<0·05$).

meat and fish consumption was also associated with higher serum Se concentrations (Table 3), whereas lower levels of serum Se were observed in male heavy consumers of vegetables and fruits (Table 3).

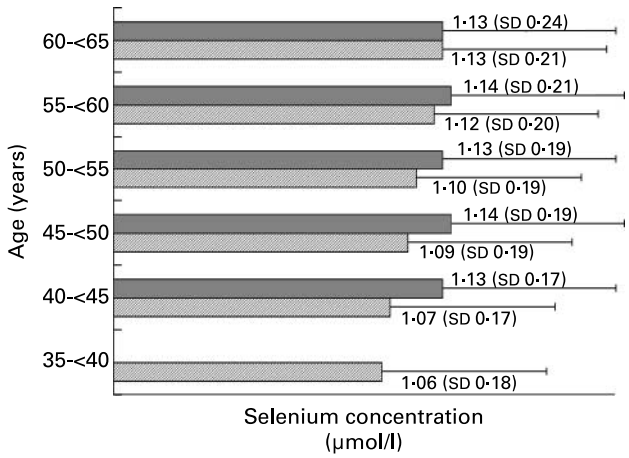

Fig. 2. Serum selenium concentrations (μmol/l) in men (■) and women (▨), depending on age. Values are means and standard deviations. Adjusted or not *P* for trend $<0·0001$ for women and $>0·89$ for men; adjustment for smoking habits, education and region.

Discussion

Epidemiological studies have suggested that low Se status is associated with an increased risk of a number of diseases, including cancer, thyroid and neurological impairment, infectious diseases and CVD (Berr, 2000; Combs, 2001; Rayman, 2002; Patrick, 2004). Thus, the assessment of Se status determinants is useful. Previous investigations on serum Se determinants yielded conflicting results, probably due to differences in the number of subjects, the geographic region and selection criteria (Robberecht & Deelstra, 1994; Alfthan & Nève, 1996). Some of the significant associations found in the present work were probably revealed because of the large sample size.

Compared to previous studies conducted in French adults, serum Se concentrations in the present study were slightly higher or else were similar (Thorling *et al.* 1986; Simonoff *et al.* 1988; Dubois *et al.* 1990; Arnaud & Preziosi, 1994). Only a very limited number of our participants had serum Se values lower than 0·75 μmol/l, the level considered to reflect inadequate Se status (Nève, 1991; Van Dael & Deelstra, 1993). However, 82·6 % of women and 74·8 % of men had a serum Se concentration below 1·25 μmol/l, the cut-off considered to be required for optimal glutathione peroxidase activity (Rayman, 1997; Nève, 2000) which confirmed that French Se intakes (Lamand *et al.* 1994) are lower than those necessary for optimal health (Nève, 2000; Broome *et al.* 2004; Thomson, 2004). Nevertheless, the present results contrast with the dramatic decrease in serum Se concentrations observed in the UK (Rayman, 1997) as a consequence of the drop in the importing of wheat from North America. Our results may be related to the non-random selection of volunteers. Although baseline characteristics of the SU.VI.M.AX participants were found to be close to the national population with regard to geographic density and socio-economic status (Hercberg *et al.* 1998), participants in the SU.VI.M.AX study may have been more aware of their nutrition than the overall French population.

The sex differences found in the present study had been previously reported in other studies (Kafai & Ganji, 2003; Niskar *et al.* 2003; Pavao *et al.* 2003), despite remaining controversial (Robberecht & Deelstra, 1994; Alfthan & Nève, 1996; Hansen *et al.* 2004). In particular, a previous study performed in French adults using similar selection criteria failed to find sex differences in serum Se concentrations (Arnaud & Preziosi, 1994). The sex difference has been attributed to differences in body weight, hormonal status and food habits (Alfthan & Nève, 1996). However, our results showed that serum Se concentrations in men were not associated with BMI, in agreement with previous studies (Telisman *et al.* 2001; Koyama *et al.* 1995), and serum Se concentrations were lower in obese women than in non-obese women, possibly because of the increased oxidative stress reported in overweight and obese people (Fenster *et al.* 2002; Keaney *et al.* 2003) or because of different eating habits. Therefore, BMI may not explain the difference between men and women in the present study. More interestingly, the increase in serum concentrations with an increase in fish, meat and alcohol consumption may contribute to the difference between genders (Alfthan & Nève, 1996), since consumption of these foods and beverages was higher in men than in women.

Table 2. Adjusted serum selenium concentrations (μmol/l) according to anthropometric and lifestyle characteristics (Mean values and standard deviations)

	Men			Women		
	Mean	SD	*n*	Mean	SD	*n*
BMI (kg/m^2)						
< 25	1·13	0·19	2335	1·09	0·22	5540
25– < 30	1·14	0·18	2000	1·09	0·20	1084
≥ 30	1·14	0·20	276	1·06	0·20	323
Adjusted *P* for trend*	0·88			0·01		
Physical activity						
Irregular	1·13	0·20	1100	1·09	0·17	1875
< 1 h/d	1·14	0·21	1212	1·08	0·20	2481
≥ 1 h/d	1·14	0·20	2407	1·09	0·21	2742
Adjusted *P* for trend*	0·32			0·26		
Smoking habits						
Never smokers	1·14	0·16	1616	1·09	0·19	3904
Former smokers	1·14	0·24	2385	1·09	0·18	2067
Light smokers (< 10 cigarettes/d)	1·14	0·20	332	1·07	0·20	602
Moderate smokers (10–20 cigarettes/d)	1·09	0·19	262	1·07	0·18	401
Heavy smokers (> 20 cigarettes/d)	1·08	0·20	142	1·05	0·19	159
Adjusted *P* for trend†	< 0·0001			0·002		
Alcohol intake (g/d)						
0	1·11	0·21	875	1·07	0·16	2909
< 15 (women) or 20 (men)	1·14	0·20	520	1·09	0·19	2185
≥ 15 (women) or 20 (men)	1·14	0·22	3087	1·11	0·19	1525
Adjusted *P* for trend*	< 0·0001			< 0·0001		

* Adjustment for age, smoking habits, education and region.
† Adjustment for age, education and region.

Hormonal status may partly explain the differences observed between sex and age. Indeed, postmenopausal women exhibited higher serum Se concentrations than premenopausal women after adjustment for age, in contrast to the results of Bergmann *et al.* (1998). However, as previously reported in Belgium (Verlinden *et al.* 1983), women taking oral contraceptives exhibited higher serum Se concentrations than other premenopausal groups. This observation is in agreement with the strong positive relationship between plasma oestrogen and plasma Se concentrations reported by Smith *et al.* (2000) in the USA. However, postmenopausal women, whether using hormonal replacement therapy or not, had similar serum Se concentrations, in agreement with previous results (Bureau *et al.* 2002). Therefore, the role of sex hormones in explaining differences between genders, and the regular increase in serum Se concentrations with increasing age in women, as reported previously (Kafai & Ganji, 2003; Pavao *et al.* 2003), remains to be elucidated (Robberecht & Deelstra, 1994). In men, serum Se concentrations were not related to age, in agreement with previous studies conducted in adults (Dubois *et al.* 1990; Robberecht & Deelstra, 1994; Telisman *et al.* 2001; Kafai & Ganji, 2003; Niskar *et al.* 2003; Pavao *et al.* 2003). The present results confirm that the decrease in serum Se concentrations with age is observed only in the elderly (Dubois *et al.* 1990; Robberecht & Deelstra, 1994; Kafai & Ganji, 2003).

Variations in serum Se concentrations according to geographic region are well known (Nève, 1991; Robberecht & Deelstra, 1994; Alfthan & Nève, 1996; Rayman, 1997; Golubkina & Alfthan, 1999; Niskar *et al.* 2003) and are related to Se intake. However, the present results contrast with reported French Se intakes (Simonoff & Simonoff, 1991). In the present study, serum Se concentrations were highest in the North and lowest in the Centre. Se intake according to the study of Simonoff & Simonoff (1991) was highest in the Southwest and the East, and lowest in Paris. The observed differences may be related to study design. Simonoff & Simonoff (1991) measured Se concentration in 200 foods and have calculated daily Se intake using Institut National de la Statistique et des Etudes Economiques food consumption tables. Men living in a rural community tended to exhibit lower Se values than those in an urban community, as previously reported in other studies (Snook *et al.* 1983; Backovic *et al.* 1999), but this remains controversial (Niskar *et al.* 2003). As in the NHANES III survey (Niskar *et al.*), serum Se concentrations were not related to urban status in women. Interestingly, in the present study the mountain regions (Centre, Alps) seemed more at risk of low serum Se concentrations than other regions. The hypothesis that consumption of fish, a good Se food source, is higher near the sea was not supported by SU.VI.M.AX results.

The influence of education and couple status on serum Se concentrations has not been extensively studied. Our present results show no evidence of a major impact of these factors, but this is not in agreement with previous studies which reported an increase in serum Se with increased education (Berr *et al.* 1998; Kilander *et al.* 2001). On the contrary, in women, the unadjusted serum Se values significantly decreased with an increase in education. The increase in serum Se in women who lived in couple, after adjustment, can be explained at least partly by an increase in meat consumption but not by differences in seafood or alcohol consumption (SU.VI.M.AX data).

Table 3. Median (25th and 75th quartiles) consumption of foods (g/d) during the first 2 years of SU.VI.M.AX (Supplémentation en Vitamines et Minéraux Antioxydants) and adjusted mean baseline serum selenium concentrations (μmol/l) according to food consumption

(Mean values and standard deviations)

	Men			Women		
	Mean (range)	SD	*n*	Mean (range)	SD	*n*
Dairy products consumption (g/d)	237 (135–353)			229 (139–345)		
< 25th percentile	1·14	0·21	662	1·09	0·18	892
25– < 50th percentiles	1·13	0·20	656	1·09	0·18	884
50– < 75th percentiles	1·12	0·21	662	1·08	0·18	892
≥ 75th percentile	1·14	0·21	661	1·09	0·18	898
Adjusted *P* for trend*	0·56			0·34		
Meat consumption (g/d)	91 (63–125)			63 (42–88)		
<25th percentile	1·10	0·20	654	1·07	0·18	884
25– < 50th percentiles	1·13	0·20	658	1·08	0·18	897
50– < 75th percentiles	1·14	0·21	663	1·10	0·18	891
≥ 75th percentile	1·16	0·21	666	1·10	0·18	894
Adjusted *P* for trend*	<0·0001			0·0001		
Fish and seafoods consumption (g/d)	40 (21–64)			32 (16–51)		
25th percentile	1·08	0·20	659	1·05	0·18	891
25– < 50th percentiles	1·12	0·20	656	1·08	0·18	883
50– < 75th percentiles	1·15	0·21	665	1·09	0·18	908
≥ 75th percentile	1·18	0·21	661	1·12	0·18	884
Adjusted *P* for trend*	<0·0001			<0·0001		
Fruits and vegetables consumption (g/d)	291 (196–404)			274 (195–373)		
25th percentile	1·14	0·21	661	1·08	0·18	887
25– < 50th percentiles	1·14	0·21	662	1·08	0·18	888
50– < 75th percentiles	1·13	0·20	658	1·09	0·18	891
≥ 75th percentile	1·12	0·21	660	1·09	0·18	900
Adjusted *P* for trend*	0·01			0·39		
Starchy foods consumption (g/d)	55 (31–90)			40 (20–65)		
<25th percentile	1·13	0·20	643	1·09	0·18	885
25– < 50th percentiles	1·14	0·21	673	1·09	0·18	891
50– < 75th percentiles	1·13	0·20	657	1·08	0·18	889
≥ 75th percentile	1·13	0·21	668	1·08	0·18	901
Adjusted *P* for trend*	0·80			0·12		
Bread and cereals consumption (g/d)	136 (94–186)			87 (60–121)		
25th percentile	1·14	0·20	653	1·09	0·18	891
25–<50th percentiles	1·13	0·20	658	1·08	0·18	888
50– < 75th percentiles	1·15	0·21	661	1·09	0·18	889
≥ 75th percentile	1·11	0·21	669	1·09	0·18	898
Adjusted *P* for trend*	0·12			0·73		
Fats consumption (g/d)	23 (16–33)			20 (14–28)		
<25th percentile	1·14	0·20	654	1·08	0·18	885
25– < 50th percentiles	1·14	0·20	658	1·09	0·18	887
50– < 75th percentiles	1·13	0·21	663	1·08	0·18	895
≥ 75th percentile	1·13	0·21	666	1·08	0·18	899
Adjusted *P* for trend*	0·27			0·61		

* Adjustment for age, education, smoking habits, region and energy intake.

Serum Se concentrations were not related to physical activity, in agreement with previous studies (Tessier *et al.* 1995; Pincemail *et al.* 2000).

The effect of smoking is controversial (Robberecht & Deelstra, 1994; Alfthan & Nève, 1996). In the present study, the decrease in serum Se concentrations was observed in smokers, in agreement with some (Hughes *et al.* 1998; Telisman *et al.* 2001; Kafai & Ganji, 2003; Niskar *et al.* 2003; Hansen *et al.* 2004; Thomson, 2004) but not all (Verlinden *et al.* 1983; Koyama *et al.* 1995; Borawska *et al.* 2004) previous studies. It has been reported that the decrease in serum Se concentrations in smokers might be related to oxidative stress (Hansen *et al.* 2004; Thomson, 2004) or to low dietary intake (Kafai & Ganji, 2003).

The increase in serum Se with a moderate increase in alcohol consumption contrasts with the decrease in serum Se concentrations reported in alcohol abusers (Robberecht & Deelstra, 1994), but a similar trend was observed in the NHANES III women (Kafai & Ganji, 2003) and suggests that moderate alcohol consumption may not adversely affect serum Se concentrations in subjects with adequate Se status (Borawska *et al.* 2004). Indeed, the decrease in Se concentrations observed in alcohol abusers has been reported to be associated with the deterioration of liver function, undernutrition (Robberecht & Deelstra, 1994; Alfthan & Nève, 1996) or moderate Se deficiency (Borawska *et al.* 2004), which is not the case in our population. Indeed, only 1·24 % men and 0·16 % women consumed more than 80 g alcohol daily,

0·5 % men and 4·4 % women were undernourished (BMI < 18·5) and less than 2 % had a serum Se concentration lower than 0·75 μmol/l. Moreover, some previous work failed to demonstrate a relationship between alcoholic beverage consumption and serum Se concentrations in middle-aged men (Koyama *et al.* 1995; Kafai & Ganji, 2003). Finally, we suggest that the increase in serum Se concentration in red wine users reflects a protective effect against oxidative stress which is counteracted in women by confounding factors.

Among the selected food groups, consumption of meat and seafood during the first 2 years of SU.VI.M.AX was strongly related to baseline serum Se concentrations. The present results are in agreement with previous studies conducted in Europe (Thorngren & Akesson, 1987; Luoma, 1998; Bergmann *et al.* 1998; Hagmar *et al.* 1998; Pavao *et al.* 2003; Hansen *et al.* 2004) and may be related both to the high Se concentrations in these foods (Zhang *et al.* 1993; Lamand *et al.* 1994, 1996; Hansen *et al.* 2004) and to good Se absorption and retention (Shi & Spallholz, 1994; Bugel *et al.* 2001, 2004; Finley *et al.* 2004) of such foods. Interestingly, Thorngren & Akesson (1987) demonstrated that an increase in fish consumption significantly increased the serum Se concentration within 3 weeks. However, this relationship was not found in Canadian fishermen (Kosatsky *et al.* 2000). In Norway, Meltzer *et al.* (1993) reported low Se bioavailability from fish, possibly due to heavy metal interactions and the nature of Se species. In contrast to seafood and meat, fruits, vegetables, starchy foods and milk contain little Se (Zhang *et al.* 1993; Lamand *et al.* 1994, 1996). Moreover, Se bioavailability from broccoli is reported to be low in rats (Finley *et al.* 2004). These low Se concentrations may explain the weak relationship between the consumption of these foods during the first 2 years of SU.VI.M.AX and baseline serum Se concentrations observed in the present study. The negative linear relationship between serum Se concentrations and consumption of fruits and vegetables, observed only in men, may be the consequence of a decrease in adequate Se food sources. The lack of a positive linear relationship between serum Se concentrations and the consumption of bread and cereals contrasts with previous data (Meltzer *et al.* 1992, 1993; Borawska *et al.* 2004). However, the positive link between serum Se concentrations and wheat consumption is more likely related to Se content, and therefore to geographic origin or to Se enrichment, than to the wheat itself (Meltzer *et al.* 1993; Golubkina & Altfhan, 1999; Djujic *et al.* 2000). In France, wheat is not a good source of Se and the concentrations of Se in bread and cereals are low (Lamand *et al.* 1994, 1996).

In conclusion, our data provide information from the first large-scale study conducted in French adults close to the French age-match population. Se status of most SU.VI.M.AX participants is not adequate for optimum selenoproteins and immune functions, and for cognitive and cancer protection (Berr, 2000; Broome *et al.* 2004; Thomson, 2004), even if the rate of biological sub-deficiency is low. We reported differences between men and women. Factors such as meat and fish consumption, smoking, moderate alcohol intake and geographic area were the main identified determinants. With respect to the key role of adequate Se status in prevention of diseases such as cancer, CVD and cognitive decline, other European large-scale intervention studies must be performed in a general population in order to determine the importance of Se status.

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