Determinants of serum levels of retinol, β-carotene and α-tocopherol in men and women born in Australia, Greece and Italy

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Serum retinol, β-carotene and α-tocopherol levels were measured in a volunteer sample of 764 Australian-, Greek- and Italian-born adult residents of Melbourne, Australia. There was no difference among the ethnic groups in mean levels of serum retinol or α-tocopherol. Mean β-carotene levels were between 11 and 22% higher for Australian-born subjects. Serum β-carotene was higher in females, retinol was higher in males. The serum levels of retinol, β-carotene and α-tocopherol were significantly positively associated with serum cholesterol. Serum triglyceride was positively associated with serum retinol and α-tocopherol but negatively associated with serum β-carotene. A positive association with retinol and an inverse association with β-carotene was found for alcohol consumption. Serum α-tocopherol was positively associated with dietary vitamin E. Serum β-carotene was correlated with carotene intake among subjects who had never smoked. Serum retinol increased with age in women only. These data provide a degree of cross-cultural robustness to previous findings in regard to the determinants of serum retinol, β-carotene and α-tocopherol in healthy men and women.

Introduction

There is some epidemiological evidence of an inverse association between the level of retinol in blood and cancer risk[1]. The suggested mechanism is that retinol inhibits tumour promotion through the regulation of cell growth and development[2]. Post-hepatic conversion to retinol is one possible mechanism that might explain a reduction in cancer risk associated with β-carotene[3], although the more conventional explanation involves its antioxidant properties[4]. Another dietary antioxidant that has been proposed to have a preventive role in the pathogenesis of cancer and coronary heart disease (CHD) is vitamin E[5].

Cross-sectional surveys in Australia show that migrants from southern Europe consume large amounts of leafy green vegetables and vegetable oils; both rich sources of antioxidants[6]. It is possible that Italian- and Greek-born Australians obtain some protection against CHD and cancer from dietary antioxidants because their mortality advantage is not explicable in terms of established risk factors such as serum cholesterol, cigarette smoking, obesity or physical inactivity[7,8].

It is well recognized that positive associations exist between the dietary intake of β-carotene and α-tocopherol and their levels in serum or plasma[9]. No such relationship is evident for retinol, although elevated serum retinol levels have been reported among individuals taking daily vitamin A supplements[10,11]. In recent years attention has focussed on identifying other factors associated with the serum levels of retinol, β-carotene and α-tocopherol. The list includes: serum cholesterol and triglycerides, age, gender, smoking status, alcohol consumption, energy intake, relative body weight, use of antihypertensive medication, and season of the year in which the blood was taken. Establishing the relative importance of the various endogenous and exogenous determinants of the level of a nutrient in serum can best be done by performing multivariate analysis with all of the independent variables included in one regression model. In addition, the extent to which the determinants are cross-culturally robust is likely to be of biological relevance yet this has not been adequately addressed. Serum levels of retinol, β-carotene and α-tocopherol were therefore measured in a field study conducted in Melbourne, the Australian city with the largest Italian and Greek communities[12]. The aims of the study were threefold: to establish whether there were differences in the serum levels of these nutrients on the basis of ethnicity; to describe a normal reference range for these nutrients in healthy Australian men and women, and to identify their determinants within a heterogeneous population using multiple linear regression.

Materials and methods

Study population and recruitment

The study population (Table 1) consisted of a volunteer sample of 764 healthy men and women who took part in the feasibility trial of the Melbourne Collaborative Cohort Study[13]. The sampling strategy was to obtain people who were likely to volunteer to be in a long-term study of their health.

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Table 1. Characteristics of the study population, n (%).

	Males			Females		
	Australian[a]	Italian[a]	Greek[a]	Australian[a]	Italian[a]	Greek[a]
Age (years)						
40–49	43 (46.7)	13 (12.6)	39 (33.1)	62 (41.6)	14 (10.5)	66 (50.0)
50–59	24 (26.1)	26 (25.2)	47 (39.8)	61 (40.9)	56 (42.1)	48 (36.4)
60–69	25 (27.2)	64 (62.1)	32 (27.1)	26 (17.4)	63 (47.4)	18 (13.6)
Smoking status						
Never smoker	43 (46.7)	32 (31.1)	30 (28.8)	104 (69.8)	108 (81.2)	99 (75.0)
Former smoker	39 (42.4)	49 (47.6)	54 (45.8)	39 (26.2)	18 (13.5)	14 (10.6)
Current smoker	10 (10.9)	22 (21.4)	34 (25.4)	6 (4.0)	7 (5.3)	19 (14.4)
Body mass index (kg/m^2)						
<20	3 (3.3)	1 (1.0)	0 (0.0)	4 (2.7)	0 (0.0)	0 (0.0)
20–24.9	26 (28.3)	9 (8.7)	23 (19.5)	70 (47.0)	21 (15.8)	28 (21.2)
25–30	56 (60.9)	74 (71.8)	75 (63.6)	57 (38.3)	62 (46.6)	81 (61.4)
>30	7 (7.6)	19 (18.4)	20 (16.9)	18 (12.1)	50 (37.6)	23 (17.4)
Use vitamin supplement at least once/week						
Multivitamin	18 (19.6)	5 (4.9)	5 (4.2)	21 (14.1)	7 (5.3)	5 (3.8)
Vitamin A	1 (1.1)	1 (1.0)	3 (2.5)	2 (1.3)	2 (1.5)	2 (1.5)
Vitamin E	2 (2.2)	4 (3.9)	1 (0.8)	10 (6.7)	4 (3.0)	2 (1.5)

[a] Refers to country of birth, most of the Italian and Greek-born participants are Australian citizens.

Participation was restricted to people living within the Melbourne Statistical Division aged between 40 and 69 years who were born in Australia or who entered Australia on a Italian or Greek passport, including some who were born in Egypt or Cyprus.

Assistance was generously provided by established networks within the Italian and Greek communities. Talks were give to church groups, regional clubs and people attending migrant resource centres. Articles were written in the ethnic, suburban and regular newspapers. Interviews were broadcast on ethnic and commercial radio programmes and awareness was spread further by word of mouth.

Recruitment of the different ethnic groups was staggered: the Greek-born subjects were recruited between November 1987 and April 1988, the Italian-born were recruited between May 1988 and July 1988 whereas the Australian-born were recruited between September 1988 and November 1988. Most of the Australian-born subjects had responded to an advertisement in a major metropolitan daily newspaper. Others responded to invitation letters which were distributed to several hundred households across Melbourne.

Study design and data collection

Upon enrolment, subjects were sent a self-administered questionnaire in their preferred language. Once this was returned every subject was visited in their home by a bilingual member of staff. As well as providing an opportunity to clarify or enter missing questionnaire responses as required, the purpose of the visit was to deliver a set of weighing scales and explain and demonstrate the procedure for recording weighed food intake. Records of weighed food intake were kept on two occasions, each of 4 days duration, at least 6 weeks apart. Subjects were asked to return the completed records by mail in pre-paid reply envelopes. The nutrient database comprised McCance and Widdowson's The Composition of Foods[14] supplemented with certain local foods[15]. The composition of some Greek composite dishes was obtained from Professor A. Trichopoulou, the author of the Greek Food Composition Table[16] and these were added together with some items created from recipes provided by the Italian and Greek subjects. The questionnaires, printed instructions and booklets for recording weighed food intake were also provided in Greek and Italian. The research instruments had earlier been pilot-tested on 40 Greek and Italian migrants.

The final data collection involved taking a 15-ml fasting blood sample and physical measurements such as blood pressure, weight, height, sitting height, body impedence, and waist and hip circumferences. Subjects were invited to attend one of 32 sessions held at ten different locations throughout Melbourne between March and April 1989. Data concerning age, country of birth, use of cigarettes, vitamin supplements and antihypertensive medication were obtained from the diet records. Body mass index (BMI, weight/height^2) was calculated from measurements of height (metres) and weight (kilograms) taken in light indoor clothing without shoes.

The study protocol was approved by the Ethics Committee of the Anti-Cancer Council of Victoria. All subjects gave their voluntary written consent before participation.

Laboratory analyses

Blood samples were obtained from fasting subjects between 7.00 and 11.00 am. From each sample, 10 ml was collected into a pre-labelled plain tube that was immediately wrapped and covered with aluminium foil. Blood samples were kept in

Table 2. Descriptive statistics of serum lipids and antioxidants.

			Mean	S.D.	Min	25th	Median	75th	Max
Cholesterol (mmol/l	Males	Italy	6.33	1.06	4.0	5.6	6.3	7.1	8.5
		Greece	6.23	1.09	3.2	5.5	6.2	7.0	9.1
		Australia	6.21	0.97	3.7	5.4	6.4	6.8	8.5
	Females	Italy	6.61	1.11	4.2	6.0	6.5	7.2	9.7
		Greece	6.26	1.03	4.3	5.5	6.3	6.9	8.9
		Australia	6.32	1.12	4.2	5.5	6.3	6.9	9.6
Triglycerides (mmol/l)	Males	Italy	2.68	3.66	0.6	1.4	1.9	2.8	33.4
		Greece	1.77	1.14	0.2	1.0	1.5	2.2	7.0
		Australia	1.70	1.04	0.4	1.0	1.4	2.1	5.1
	Females	Italy	1.84	1.03	0.5	1.1	1.5	2.3	6.1
		Greece	1.39	0.75	0.4	0.8	1.2	1.7	4.0
		Australia	1.27	0.70	0.4	0.8	1.0	1.5	4.9
Retinol (μmol/l)	Males	Italy	2.99	0.88	1.2	2.5	2.9	3.4	6.8
		Greece	2.97	0.97	0.9	2.4	2.8	3.4	6.1
		Australia	3.06	0.86	0.9	2.5	3.1	3.5	6.8
	Females	Italy	2.71	0.78	0.9	2.2	2.7	3.1	6.4
		Greece	2.53	0.94	0.9	1.8	2.4	3.1	5.3
		Australia	2.68	0.86	0.8	2.1	2.6	3.1	6.0
β-carotene (μmol/l)	Males	Italy	0.79	0.59	0.1	0.4	0.7	0.9	4.6
		Greece	0.72	0.43	0.1	0.4	0.6	0.8	3.2
		Australia	0.92	0.58	0.2	0.5	0.8	1.2	3.6
	Females	Italy	1.01	0.52	0.1	0.7	0.9	1.3	2.7
		Greece	0.99	0.56	0.2	0.6	0.9	1.3	3.4
		Australia	1.11	0.61	0.2	0.7	1.1	1.4	3.2
α-tocopherol (μmol/l)	Males	Italy	35.0	14.6	10	24	32	43	94
		Greece	33.3	11.4	7	25	31	39	70
		Australia	32.7	12.2	9	27	31	39	89
	Females	Italy	32.7	11.2	9	25	32	37	73
		Greece	33.5	12.8	11	23	32	41	80
		Australia	32.4	12.3	1	25	31	38	98

the dark and allowed to clot at room temperature before being transferred on ice to the laboratory within 3–4 h of phlebotomy. The samples were centrifuged and the serum removed and stored at –80°C for up to 3 months.

Serum retinol, β-carotene and α-tocopherol were measured by a commercial laboratory using reverse-phase high-performance liquid chromatography. Serum total cholesterol and triglyceride concentrations were determined using enzymatic colorimetric reagents on a Roche Cobas Fara auto-analyser by the Biochemistry Department of the Alfred Hospital, Melbourne.

Statistical analyses

For descriptive purposes, medians, means and standard deviations were computed on untransformed variables. We did not pursue tests of statistical significance relating to ethnic differences in anthropometric, dietary or serum measurements because of the nonprobabilistic nature of the survey sample. Linear regression procedures were used in analysing the determinants of serum retinol, β-carotene and α-tocopherol. All continuous variables that exhibited a log-normal distribution were transformed by the natural logarithm to improve normality prior to regression and correlation analysis. Alcohol and BMI were the only continuous variables that were not transformed. Sex, age, ethnicity and cigarette smoking status were entered as indicator variables in the multiple linear regression models. Dietary carotene, vitamin E and alcohol were adjusted for energy as the residuals from the regression model on the log scale plus the expected nutrient intake for the mean energy intake of the study population[17]. Results were considered significant for two-tailed P values less than 0.05.

Results

Selected characteristics of the study population are shown in Table 1. Descriptive statistics of serum lipids and micronutrients are given in Table 2. Serum β-carotene was higher in females than males in each ethnic group. Mean β-carotene levels were between 11 and 22% higher for Australian-born men and women than for subjects born in Italy and Greece. There was about a six-fold range in serum retinol in this sample of healthy men and women. In contrast to serum retinol, which is subject to homoeostatic control,the distribution of serum β-carotene was highly skewed. The interquartile range was only two-fold but the overall range of values observed was at least 20-fold.

The distribution profiles of serum α-tocopherol stratified by sex and ethnicity were very similar. There was an approx-

Table 3. Pearson correlation coefficients.

	Males (n = 313)			Females (n = 414)		
	β-carotene (μmol/l)	Retinol (μmol/l)	α-tocopherol (μmol/l)	β-carotene (μmol/l)	Retinol (μmol/l)	α-tocopherol (μmol/l)
Age (years)	0.00	–0.04	0.08	0.00	0.15	0.09
*Smoking (cigarettes/day)	–0.04	–0.02	0.03	–0.25	0.05	0.14
*Alcohol (g/day)	–0.12	0.06	–0.02	0.18	0.01	–0.07
BMI (kg/m^2)	–0.05	0.03	–0.04	–0.17	0.03	–0.01
Serum cholesterol (mmol/l)	0.00	0.29	0.40	0.06	0.18	0.45
Serum triglyceride (mmol/l)	–0.06	0.21	0.38	–0.18	0.24	0.24
Energy intake (kJ/day)	0.07	0.05	0.04	–0.11	0.00	–0.03
Dietary carotene (mg/day)	0.08	0.00	0.02	0.10	0.00	0.01
Dietary retinol (mg/day)	0.04	–0.03	0.04	0.10	–0.06	–0.03
Dietary vitamin E (mg/day)	0.06	0.06	0.13	0.15	–0.04	0.04

* correlations are over smokers only (n = 202 m, 102 f) for cigarettes and drinkers only (n = 237 m and 141 f) for alcohol.

Table 4. Predictors of serum retinol, β-carotene and α-tocopherol in multiple regression analyses.

Dependent variable	Explanatory variable	Regression coefficient Estimate	95% confidence interval		Multiple R^2
Serum retinol (μmol/l)	(Intercept)	0.32	0.07	0.58	13%
	sex	–0.08	–0.13	–0.02	
	log (cholesterol)	0.33	0.19	0.47	
	log (triglyceride)	0.10	0.06	0.15	
	alcohol<10g/d	0.04	–0.02	0.10	
	alcohol>10g/d	0.11	0.04	0.17	
Serum retinol (μmol/l)	(Intercept)	0.44	0.09	0.79	11%
Females only	log (cholesterol)	0.20	0.00	0.39	
	log (triglyceride)	0.13	0.07	0.20	
	age 50–60	0.07	–0.01	0.14	
	age 60–70	0.08	0.00	0.17	
	alcohol<10g/d	0.02	–0.05	0.09	
	alcohol>10g/d	0.14	0.06	0.23	
Serum β-carotene (μmol/l)	(Intercept)	0.03	–1.37	1.43	13%
	log (dietary carotene)	–0.11	–0.28	0.06	
	sex	0.16	0.06	0.27	
	past smoker	–1.03	–2.60	0.55	
	never smoker	–1.66	–3.12	–0.19	
	BMI	–0.01	–0.02	0.00	
	log (triglyceride)	–0.19	–0.28	–0.10	
	log (cholesterol)	0.38	0.12	0.64	
	Greek-born	–0.09	–0.19	0.02	
	Australian-born	0.03	–0.09	0.14	
	alcohol<10g/d	–0.04	–0.15	0.07	
	alcohol>10g/d	–0.12	–0.24	0.00	
	log (dietary carotene) past smoker	0.16	–0.04	0.36	
	log (dietary carotene) never smoker	0.24	0.05	0.42	
Serum α-tocopherol (μmol/l)	(Intercept)	2.07	1.76	2.37	23%
	log (cholesterol)	0.82	0.68	0.96	
	vitamin E supplements	0.26	0.39	0.13	
	log (triglyceride)	0.10	0.05	0.14	
	log (dietary vitamin E)	0.07	0.01	0.13	

imately 10-fold range of observed values, excluding the minimum serum α-tocopherol value for an Australian-born woman. There was no obvious explanation of this deficient value; the subject had no clinical evidence of vitamin E deficiency and her dietary intake of vitamin E was normal.

There was no appreciable difference in serum cholesterol values on the basis of sex or ethnicity. However, median serum triglyceride values were higher among Italian-born men and women.

Pearson correlation coefficients between the serum levels of β-carotene, retinol and α-tocopherol and selected personal characteristics and dietary intake variables are presented in Table 3. The strongest correlations were with serum lipids. Cholesterol and triglycerides were positively correlated with serum retinol and α-tocopherol. Serum β-carotene was inversely correlated with triglycerides. There was a modest positive association between dietary carotene and serum β-carotene in both men and women. Similarly dietary vitamin E was correlated with serum α-tocopherol. There was a weak inverse association between the retinol content of the diet and its level in serum. Male sex and serum cholesterol and triglycerides were significant determinants of serum retinol in the multiple regression model (Table 4). Alcohol was the only other variable that was positively associated with serum retinol in both men and women. Variables not independently associated with serum retinol were: dietary retinol, vitamin A supplements, antihypertensive medication, BMI, smoking, ethnicity and age. Although age was not a significant predictor of serum retinol in the regression model, we included age in a separate regression model for women as there was a significant progression in serum retinol with age in women (Figure 1). Levels were intermediate in the perimenopausal age range so a dichotomous variable, pre- or postmenopause, was entered into the regression model. In contrast to age, menopausal status was not a clear predictor of the level of serum retinol in women.

Serum β-carotene was positively associated with female sex and serum cholesterol. A significant association between dietary carotene and serum β-carotene was restricted to people who had never smoked. Factors associated with a significant reduction in serum β-carotene included serum triglycerides, alcohol consumption, and current and past history of cigarette smoking. Greek ethnicity was also independently associated with a reduction in serum β-carotene.

Three factors were identified as strong independent predictors of serum α-tocopherol: cholesterol, triglycerides and use

Table 5. Existing reference levels of blood retinol, β-carotene and α-tocopherol in Australian and Italian adults

Year	First author	Subjects		Country	Age[a]	Sex	Sample	Mean	S.D.
Retinol (μmol/l)									
1988	Brock[19]	143	population controls	Australia	18 – 65	F	plasma	1.94	–
1989	Wahlqvist[20]	10	–	Australia	37 ± 9	M	serum	3.55	0.63
1989	Wahlqvist[20]	11	–	Australia	35 ± 13	F	serum	3.25	0.73
1989	Kune[21]	63	hospital controls	Australia	66.6 ± 8.5	M	serum	1.99	0.53
1991	Rabuco[22]	5	Australian Aborigines	Australia	18 – 32	F	plasma	1.43	–
1991	Rabuco[22]	3	Non Aboriginals	Australia	25 – 38	F	plasma	1.78	–
1991	Rabuco[22]	3	Non Aboriginals	Australia	25 –38	M	plasma	1.85	–
1992	Kune[23]	88	surgical controls	Australia	65 ± 7	M	serum	2.51	0.98
1984	Fidanza[24]	39	aged pensioners in Perugia	Italy	65 – 69	M	plasma	2.34[b]	–
1984	Fidanza[24]	55	aged pensioners in Perugia	Italy	65 – 69	F	plasma	2.00[b]	–
1987	Porrini[25]	75	residents of a small town	Italy	60 – 69	F	plasma	1.74	0.53
1987	Porrini[25]	18	residents of an agricultural village	Italy	60 – 69	F	plasma	1.33	0.53
1987	Porrini[25]	52	residents of a small town	Italy	60 – 69	M	plasma	1.91	0.71
1988	Gerber[26]	209	hospital controls	Italy	30 – 65	F	plasma	1.85	0.50
β-carotene (μmol/l)									
1988	Brock[19]	143	population controls	Australia	18 – 65	F	plasma	0.56	–
1989	Kune[21]	63	hospital controls	Australia	66.6 ± 8.5	M	serum	1.57	0.49
1990	Bain[27]	62	baseline – intervention group	Australia	56 ± 10.8	39 M 23 F	serum	0.56	0.37
1990	Bain[27]	60	baseline – placebo group	Australia	55 ± 9.7	37 M 23 F	serum	0.50	0.31
1991	Rabuco[22]	5	Australian Aborigines	Australia	18 – 32	F	plasma	0.45	–
1991	Rabuco[22]	3	Non Aboriginals	Australia	25 – 38	F	plasma	1.34	–
1991	Rabuco[22]	3	Non Aboriginals	Australia	25 – 38	M	plasma	1.25	–
1992	Kune[23]	88	surgical controls	Australia	65 ± 7	M	serum	1.66	0.45
1992	Wattanapenpaiboon[28]	20	Caucasians	Australia	47.2 ± 6.3	F	serum	0.40	–
1988	Gerber[26]	209	hospital controls	Italy	30 –65	F	plasma	0.75	0.41
α-tocopherol (μmol/l)									
1990	Silbert[29]	9	non-medical hospital workers	Australia	41 – 63	M	plasma	25.0	6.0
1991	Lo[30]	14	–	Australia	–	M	serum	27.56	3.74
1991	Lo[30]	14	–	Australia	–	F	serum	27.98	8.51
1987	Porrini[25]	75	residents of a small town	Italy	60 – 69	F	plasma	27.86	9.29
1987	Porrini[25]	18	residents of an agricultural village	Italy	60 – 69	F	plasma	30.18	6.97
1987	Porrini[25]	52	residents of a small town	Italy	60 – 69	M	plasma	25.54	11.61
1988	Gerber[26]	209	hospital controls	Italy	30 – 65	F	plasma	25.31	6.20
1989	Rubba[31]	74	residents of Sapri	Italy	40 – 49	M	plasma	25.1	7.0
1990	Riemersma[32]	80	apparently healthy men	Italy	40 – 49	M	plasma	23.9[b]	–

[a] Age is expressed as mean ± SD or range [b] median

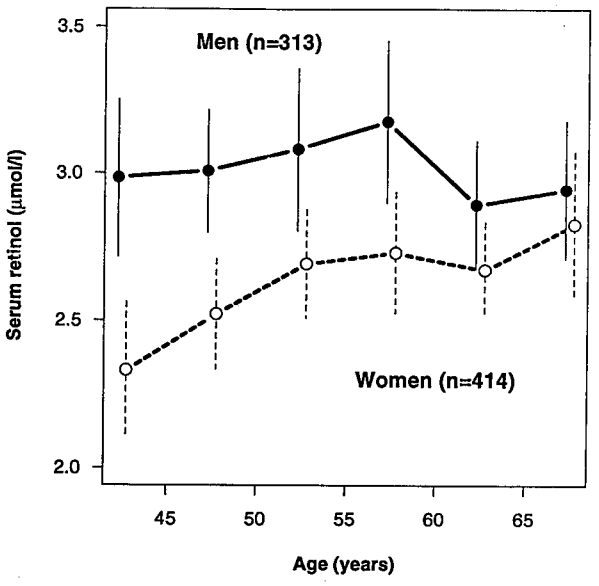

Figure 1. Convergence of male and female serum retinol levels with age.

of vitamin E supplements. Dietary vitamin E was another significant determinant of serum α-tocopherol, but only after two outliers were removed from the analysis.

Discussion

Nutrients with antioxidant properties are currently the focus of considerable research activity as they are thought to offer some protection against CHD and certain forms of cancer. Optimal plasma levels have recently been suggested: retinol >2.2-2.8 μmol/l, β-carotene > 0.4–0.5 μmol/l and α-tocopherol >27.5–30.0 μmol/l[18]. The existing literature relating to average blood levels of these antioxidants in Australian and Italian adults is more confusing than illuminating; there is little consistency in mean values even when reported from the same laboratories (Table 5). The present study involved a non-random sample so it is not suitable for establishing the prevalence of suboptimal antioxidant nutrient status in the general population. However, as the largest study of its type to have been conducted in Australia it can be used as a reference range.

The low proportion of current cigarette smokers among the Australian-born suggests that they may have been more health-conscious than the general population. Conversely, the high proportion of Italian- and Greek-born subjects who were overweight or obese suggests that they were less likely to have experienced this particular bias. Comparisons on the basis of ethnicity were further complicated by the different age structures of the sub-groups. Serum levels of retinol were higher in males than females in each ethnic group (Table 2). However, the difference was smallest among the Italian-born who had a far higher proportion over 60 years of age.

The observation that the Australian-born participants had relatively higher levels of serum β-carotene must be treated cautiously. Carrots are the richest source of β-carotene in the diet and men and women born in Australia have been shown to eat substantially more carrots than do migrants from southern Europe[33]. β-carotene is not the only carotenoid with antioxidant properties and it is possible that southern European migrants have a greater overall carotenoid intake than do native-born Australians. Italian and Greek-born migrants eat more tomatoes and leafy green vegetables[33] and these foods respectively contain lycopene and xanthophyll as well as many other flavonoids[34]. Future studies of this type should test a boarder range of carotenoids in serum such as α-carotene, lycopene, lutein, cryptoxanthin, phytoene and zeaxanthin. Greek ethnicity was a significant inverse predictor of serum β-carotene independently of diet and other lifestyle factors and personal characteristics. This might be explained by the fact that during the two months when the blood samples were taken many of the Greek-born subjects were observing Lenten fasting according to the rituals of the Orthodox religion.

Sex was an independent determinant of serum levels of retinol and β-carotene but not α-tocopherol in our study. This is consistent with most studies of this type[35–40] although a large Finnish study reported higher α-tocopherol levels in women[41].

Numerous studies in young and middle-aged adults have found that serum retinol levels are higher in males than females[11, 42]. However, no difference in serum retinol levels between the sexes have been found in studies conducted among the elderly[43]. For this to be the case, there must be an increase in serum retinol with age in women and/or a reduction in serum retinol with age in men. A differential effect in men and women might explain why there is inconsistency in the literature whether serum retinol levels increase with age[11, 36, 44]. An earlier study had found a strong correlation between serum retinol and age in women only[39]. We also found a significant progression in serum retinol with age in women (Figure 1) so we included age and menopausal status in a separate regression model for women. Menopausal status was not found to be an independent determinant of serum retinol in the linear regression model. However, as menopausal status is highly correlated with age, the possibility that it might be biologically important can not be completely excluded.

Two Japanese studies have shown an increase in plasma β-carotene with age[35, 38] but no other study has shown such a relationship[10, 11, 37, 39, 42, 45, 46]. There was no effect of age on the level of serum β-carotene or α-tocopherol in the present study. Serum cholesterol was a significant predictor of serum retinol, β-carotene and α-tocopherol in our regression models. Positive correlations of a similar magnitude have been found in many studies conducted in different population settings[39, 41, 44, 46, 47]. We found an inverse association between serum triglycerides and β-carotene and positive correlations with retinol and α-tocopherol. The inverse association with β-carotene was found in three studies [37, 39, 46] although only among women in the study of Ascherio et al[39] and no association was found in another study[45]. Reasonably strong positive correlations between serum triglycerides and both retinol and α-tocopherol have been described previously[37, 39, 44, 46].

Cigarette smoking was inversely associated with serum β-carotene but not with retinol or α-tocopherol. Smoking status was a significant determinant of serum β-carotene in the multivariable regression model. In contrast to the study of Nierenberg et al[11] where there was no difference in the relationship between dietary and plasma β-carotene among smokers and non-smokers, we found an interaction, similar to that which had been described by many others[10, 37, 40, 48, 49].

Among current and past smokers the relationship between dietary and serum β-carotene was weak and not significant, whereas there was a significant correlation among subjects who had never smoked. The Pearson product–moment correlation coefficient between dietary and serum β-carotene among non-smokers in the present study (r=0.11) was lower than has been reported in comparable studies which have used validated food frequency questionnaires that enquire about usual intake in the preceding 12 months[37, 49]. We measured actual food intake for a total of 8 days over a period up to 18 months prior to blood collection. There is limited information available regarding the minimum number of days required to characterize an individual's habitual intake of β-carotene, but the literature concerning vitamin A indicates that it may considerably exceed 8 days[50].

Consistent with most other studies[10, 35, 38, 45] we found an independent inverse effect of alcohol consumption on serum β-carotene in multivariate analysis. One study found no effect[39] and another found an effect of alcohol only among males[37]. The positive association we found in univariate analysis between alcohol and serum β-carotene in women was driven by one outlier. As has been found in several previous studies[10, 39, 45] alcohol was positively associated with serum retinol in both males and females. There was no effect of alcohol on serum α-tocopherol.

Notwithstanding the fact that only 23 subjects claimed they regularly took vitamin E supplements, this indicator variable was a significant predictor of the level of serum α-tocopherol in the linear regression model. We were unable to calculate total vitamin E intake because we did not collect details of the dose of vitamin supplements used. Two studies that have measured total vitamin E intake found substantially stronger correlations among those who took vitamin E supplements compared to those who did not[37,39]. In univariate analysis an inverse correlation was observed between BMI and serum β-carotene, but this disappeared once serum lipids were added to the regression model. We were unable to study the effect of seasonal factors as all blood samples were collected in the space of 2 months during autumn. A number of other factors have been associated with the serum level of β-carotene in other studies, including energy intake[45], use of multi-vitamin supplements[42] and antihypertensive medication[11] but none of these was found to have an independent effect in the present study.

In summary, this study has corroborated previous findings in regard to the determinants of serum retinol, β-carotene and α-tocopherol. The distribution profiles for these antioxidants can serve as Australian reference values. Our data do not support the hypothesis that vitamins A and E are responsible for the protection experienced by southern European migrants against CHD and cancers of the colon, rectum, breast and prostate. However, a more appropriate study design would involve a longitudinal study which included an ethnically diverse cohort.

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Determinants of serum levels of retinol, β-carotene and α-tocopherol in men and women born in Australia, Greece and Italy

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澳大利亞、希臘和意大利出生的男子和婦女血清視黃醇、β－葫蘿白素和α－生育酚水平的決定因素

摘要

作者在澳大利亞墨爾本選用了 764 位自願的澳洲、希臘和意大利出生的成人居民爲對象，測定了他們血清視黃醇、β－葫蘿白素和α－生育酚的水平。結果發現：血清視黃醇或α－生育酚平均水平沒有明顯的種族差異。澳洲出生者的β－葫蘿白素平均水平高出 11—22 %。血清β－葫蘿白素水平在女性較高，而視黃醇則男性較高。血清膽固醇與血清視黃醇、β－葫蘿白素和α－生育酚呈明顯正相關。血清甘油三酯與血清視黃醇和α－生育酚呈正相關，但與血清β－葫蘿白素呈負相關。飲酒與血清視黃醇呈正相關，但與β－葫蘿白素呈負相關。血清α－生育酚與膳食維生素E呈正相關。不吸煙者血清β－葫蘿白素與葫蘿白素進食量呈正相關。婦女血清視黃醇隨年齡而增加。這些數據在一定程度上，提供了不同種族男女血清視黃醇、β－葫蘿白素和α－生育酚水平的決定因素。