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Prevalence of anemia in elderly subjects living at home: role of micronutrient deficiency and inflammation

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Objective: Aging is associated with increased risk of developing anemia and micronutrient deficiencies. Wheat-based staple foods are iron fortified in Chile. We aimed to establish the prevalence and etiology of anemia in apparently healthy free-living elderly subjects.

Design and setting: A cross-sectional study was performed in an outpatient clinic of Santiago, Chile.

Subjects and methods: A group of 274 subjects (93 men, 181 women) \geq 60 y old living at home and apparently healthy was studied. Clinical and anthropometric evaluations and dietary survey were performed. Complete blood count, and status of iron, copper, folate, vitamins B₁₂ and A and C-reactive protein, and erythrocyte sedimentation rate were measured.

Results: Prevalence of anemia was 5.4% for men and 4.4% for women. Subjects with inflammatory process had a higher prevalence of anemia (22.2% men, 31.6% women). Abnormal serum retinol (<0.35 μ mol/l) was found in 13.7% of men and 15.9% of women. Prevalence of folate deficiency (<7 nmol/l) was 50.5% in men and 33.1% in women. Low serum vitamin B₁₂ (<148 pmol/l) was present in 51.1% of men and 30.9% of women. Iron and copper deficiencies were infrequent.

Conclusions: Anemia is not prevalent in free-living elderly subjects when iron intake is adequate. Inflammatory process is the main etiology of anemia in this age group. Vitamin A, folate and vitamin B_{12} deficiencies were found in a significant proportion of the study group.

Sponsorship: Sandoz Foundation for Gerontological Research.

Descriptors: elderly; anemia; inflammation; iron; copper; vitamin A; folate; vitamin B₁₂

European Journal of Clinical Nutrition (2000) 54, 834-839

Introduction

The increase in life expectancy is a worldwide phenomenon that has led to a progressive increase in the number of elderly persons over the past 50 y. It is estimated that in Chile the proportion of adults older than 60 y of age will increase from 10% in 1999 to 16% in 2050.

The function of some organs and systems is decreased by the aging process. An age-related decline in gastrointestinal and bone marrow functional reserves has been found to occur among the elderly (Lipschitz et al, 1984; Russell, 1992). The elderly have decreased physical activity, changed dietary patterns and, in developing countries, a lowered food supply due to socioeconomic factors. This population group has also an increased frequency of inflammatory processes. These factors make the elderly more prone to developing anemia and micronutrient deficiencies which affect erythropoiesis. The principal nutritional causes of anemia are iron, folate and vitamin B₁₂ deficiencies, and protein energy malnutrition (Lipschitz et al, 1981; Mansouri & Lipschitz, 1992; Yip & Dallman, 1988). The relative contribution of inflammatory diseases and nutritional causes varies among different studies.

Epidemiological studies come mainly from industrialized countries, particularly from institutionalized elderly patients. In a compilation of the prevalence of anemia in different regions of the world published in 1985 (DeMaeyer & Adiels-Tegman, 1985), the prevalence of anemia was found to be 12% and 18–65% in developed and less developed regions, respectively. However, the prevalence and etiology of anemia in free-living elderly people of developing countries is not well established.

The purpose of this study was to establish the prevalence and etiology of nutritional anemia in free-living 'apparently healthy' elderly subjects living in an urban community of Santiago—Chile.

Subjects and methods

A group of 274 free-living subjects (93 men and 181 women) \geq 60 y old and apparently healthy was recruited from the population assigned to one outpatient clinic corresponding to a low-socioeconomic-level district in the city of Santiago, Chile. Ninety-five percent of the population of Santiago lives in urban areas and 5% in rural areas. Seventeen percent of the inhabitants of the selected district were \geq 60 y old. The population of this district had good access to public utilities, with 100% of homes having electricity, running water and sewage connections. The elderly mortality rate was 36.8 per 1000 subjects \geq 60 y old. There was no information on the prevalence of infections or chronic diseases. 'Apparently healthy' is defined as being free of acute or chronic disease as determined by the medical history and physical examination. Furthermore,

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Contributors: The paper was written primarily by MO and EH with the assistance of the other authors. All authors contributed to the design, implementation of the study, analysis and discussion of the results of the study, and approved the final version of the manuscript.

Received 21 January 2000; revised 13 April 2000; accepted 9 August 2000

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none of the subjects had been hospitalized or received supplementation with iron, copper, folate vitamin B_{12} , vitamin A or drugs that modify erythropoiesis within the previous 6 months.

A physician examined all subjects, and anthropometric measurements were taken by a research dietitian. Weight was measured to the nearest 0.1 kg using a weighing scale (SECA, Hamburg, Germany). Height was measured to the nearest 0.5 cm using a custom-made stadiometer. Individuals selected were visited at their homes by a trained research dietitian to apply two 24 h recall questionnaires 7-10 days apart. A food frequency questionnaire was obtained on the same occasion of the first 24 h recall. Assistance by the spouse or a relative was provided to help the respondent recall their usual intake. The 24 h recall questionnaire consisted of a conversation identifying in detail what foodstuffs, dishes and snacks had been eaten and how much, during the preceding day. The interview progressed in chronological order, beginning with the first meal eaten by the subject. All the foodstuffs and dishes and their amounts were recorded meal by meal. The interviewee was allowed to designate freely the size of the servings by units of weight, volume or household measures, with or without the aid of food models. For the food frequency consumption questionnaire, respondents were asked about their usual food consumption over the past month going through a 90 food item list. The interview progressed according to food groups. As for the 24h recall questionnaire, food models and common household measures were utilized in the quantitative estimation. The interviewee reported the frequencies of the different foods per day, per week, or per month. Individual foods eaten less frequently than once a month were not recorded. Food items were coded and nutrient intake was computed by Microsoft® Excel 97 software using Chilean food tables as the primary database (Schmidt-Hebbel et al, 1992), supplemented with information from the USDA nutrient database (USDA, 1998) for those nutrients in which the Chilean tables were incomplete. The 24h recall method has been validated in our laboratory comparing calculated and actually measured (by chemical analyses) copper, zinc and iron intakes (Pederneiras, 1998).

A fasting venous blood sample was obtained from an antecubital vein to measure: erythrocyte count, hemoglobin (Hb), mean red cell volume (MCV), leukocyte count (Coulter Counter ZBI, Hialeah, FL), serum iron (Fe), total iron binding capacity (TIBC), transferrin saturation (Sat) (Fisher & Price, 1964), free erythrocyte protoporphyrin (FEP) (AVIV hematofluorimeter, Lakewood, NJ), serum ferritin (SF) (INACG, 1985), serum folate, serum vitamin B₁₂ (Simultrac kit, Becton Dickinson, Orangeburg, NY), serum retinol (Thompson et al, 1971), serum copper (Cu) (atomic absorption spectrophotometer, Perkin Elmer 2280, Norwalk, Conn), serum albumin, urea nitrogen, total cholesterol plasma glucose (Wiener Laboratories, Rosario, Argentina), C-reactive protein (CRP) (Turbox, Espoo, Finland) and erythrocyte sedimentation rate (ESR). In all anemic subjects gastrointestinal blood losses were measured with the modified quantitative stool hemoglobin procedure according to Schwartz et al (1983).

The cut-off values used to define abnormal hematological and biochemical measurements were: anemia, Hb < 130 g/l and 120 g/l for men and women, respectively; microcytosis, MCV < 80 fl and macrocytosis, MCV > 100 fl; abnormal iron status parameters were set at Sat< 16%, FEP > 1.77 μ mol/l rbc, SF < 12 μ g/l; insufficient iron stores, SF < $20 \,\mu\text{g/l}$; copper deficiency, Cu < $11.0 \,\mu\text{mol/l}$; vitamin A deficiency, serum retinol < 0.35 μmol/l, and low vitamin A levels, serum retinol < 0.70 μmol/l; folate deficiency, serum folate < 7 nmol/l; and vitamin B₁₂ deficiency, $< 74 \, \text{pmol/l}$, and low vitamin B_{12} levels, $< 148 \,\mathrm{pmol/l}$.

Ten percent of men and 11% of women demonstrated evidence of an inflammatory process, identified by at least one abnormal value among the four laboratory indicators of inflammation (white cell count > 11×10^9 /l, band count > $0.5 \times 10^9/1$, erythrocyte sedimentation > 40 mm/h, and C-reactive protein > 12 mg/dl).

Because serum ferritin, serum folate and serum vitamin B₁₂ concentrations have a skewed distribution, they were converted to logarithms before performing mean and s.d. analysis; the results were retransformed to antilogarithms to recover the original units and expressed as geometric means and ± 1 s.d. ranges. Statistical analysis included Student's t-test, ANOVA, chi-square test, and Pearson's correlation. When ANOVA was statistically significant, identification of significant differences between groups was based on Scheffé's post hoc test. Statistical analyses were performed by the program Statistica for Windows, release 4.5, StatSoft Inc., Tulsa, OK.

Written informed consent of the subjects was obtained before inclusion in the study, and the protocol was approved by the Ethics in Human Research Committee of the Institute of Nutrition and Food Technology of the University of Chile, which supervises the use of humans as experimental subjects.

Results

Mean age and range were 70.1 ± 6.7 y (range 60-89 y) and 70.2 ± 6.7 y (range 60-93 y) for men and women, respectively. The age distribution was similar in both sexes, although the number of women was higher. There were significant differences in the marital status between men and women (Chi-square test P < 0.001). The distribution for men was: single 6.5%; married 74.2%; divorced 3.2%; and widowed 16.1%. The corresponding figures for women were: single 18.2%; married 29.8%; divorced 7.2%; and widowed 44.8%.

Mean weight, height and body mass index were $68.9 \pm 10 \,\mathrm{kg}$, $1.62 \pm 0.1 \,\mathrm{m}$ and $26.1 \pm 4.1 \,\mathrm{kg/m^2}$ for men and $62.3 \pm 14 \,\mathrm{kg}$, $1.50 \pm 0.1 \,\mathrm{m}$ and $27.7 \pm 6.1 \,\mathrm{kg/m^2}$ for women.

Since ANOVA analysis revealed no statistically significant differences in the results obtained with the three dietary surveys performed, individual nutrient intake was calculated as a mean of the two 24h recalls and the food frequency questionnaire. Women presented significantly lower daily dietary intakes per kg body weight in energy, proteins, lipids, iron and copper (Table 1). A significantly higher percentage of women had iron, copper and vitamin A daily intakes below 75% of the US NAS-NRC FNB recommendations (Table 2) (NRC, 1989).

There were significant differences between men and women in all hematological and biochemical measurements except for serum retinol (Table 3). However, the prevalence of anemia, abnormal iron status parameters, low serum copper and deficient serum vitamin B_{12} values was very low in both sexes. There was an inverse correlation between hemoglobin and age in men (r = -0.21,P < 0.05) and women (r = -0.17, P < 0.03). Reduced



Table 1 Daily dietary intake in apparently healthy men and women \geq 60 y old

	Men (n = 93)	Women (n = 181)	Student's t-test P
Energy			
kJ	7627 ± 2297	5791 ± 1883	< 0.001
kJ/kg ^a	114.5 ± 28.3	104.5 ± 36.4	< 0.02
Protein			
g	60.5 ± 23.1	46.5 ± 22.1	< 0.001
g/kg	0.9 ± 0.3	0.8 ± 0.4	< 0.03
Lipids			
g	46.2 ± 22.8	33.6 ± 17.6	< 0.001
g/kg	0.7 ± 0.2	0.6 ± 0.3	< 0.002
Carbohydrates			
g	286.2 ± 83.0	227.6 ± 76.7	< 0.001
g/kg	4.3 ± 1.2	4.1 ± 1.5	NS
Iron			
mg	16.3 ± 4.8	12.8 ± 4.6	< 0.001
mg/kg	0.24 ± 0.08	0.21 ± 0.09	< 0.006
Copper			
mg	1.4 ± 1.0	1.0 ± 0.5	< 0.001
mg/kg	0.021 ± 0.015	0.017 ± 0.009	< 0.02
Vitamin A			
μg RE	852 ± 2037	561 ± 768	NS
μ RE/kg	12.6 ± 30.4	9.9 ± 14.9	NS
Folate			
μg	214 ± 67	182 ± 72	< 0.001
μg/kg	3.2 ± 1.0	3.1 ± 1.4	NS
Vitamin B ₁₂			
μg	4.4 ± 9.3	2.3 ± 3.5	< 0.05
μg/kg	0.064 ± 0.139	0.041 ± 0.067	NS

^aNutrient intake per kg body weight.

serum retinol values was found in 34.2% of men and 29.0% of women. The corresponding figure for deficient serum retinol values was 13.7% and 15.9%. A high prevalence of abnormal serum folate levels and low vitamin B₁₂ values was found in both genders. Both micronutrient deficits were significantly more prevalent in men.

Dietary intake of micronutrients was not correlated with micronutrient blood levels. However, retinol intake was significantly correlated with serum retinol in women (r = 0.18, P < 0.03).

Table 2 Percentage of subjects below 75% of the recommended dietary

	Men $(n = 93)$	Women $(n = 181)$	χ^2
Energy	37.6	49.7	NS
Protein	19.4	25.4	NS
Iron	1.1	8.3	< 0.04
Copper ^a	24.7	61.9	< 0.0001
Vitamin A	83.9	70.2	< 0.03
Folate	14.0	22.7	NS
Vitamin B ₁₂	34.4	44.8	NS

^aBelow low limit of estimated safe and adequate daily dietary intake.

In both sexes, the prevalence of anemia was significantly higher in subjects with laboratory evidence of inflammation (P < 0.0001). Anemia was found in 22.2% of men and 31.6% of women with inflammation, while the prevalence of anemia without inflammation was 4.8% in men and 1.3% in women.

The hematological and biochemical characteristics of the anemic subjects are presented in Table 4. Eight of the anemic subjects had laboratory evidences of an inflammatory process, and four subjects had low serum folate levels.

Discussion

The prevalence of anemia in free living elderly subjects was very low. Hemoglobin below the cut-off point recommended by WHO was found in 5.4% and 4.4% of aged men and women, respectively. These percentages are slightly higher in men and slightly lower in women to those found in adults 18-44 y old from a national sample (1.1% in men and 8.4% in women) (Ríos et al, 1983).

Iron deficiency is the main cause of anemia worldwide (DeMaeyer & Adiels-Tegman, 1985). Anemia is due mostly to a low iron intake and/or a low bioavailability of dietary iron. However, inflammation and chronic blood loss, predominantly from the gastrointestinal tract, are frequent etiologies of anemia in the elderly, especially in developed countries (Stander, 1989; Yip & Dallman, 1988).

Table 3 Hematological and biochemical measurements in apparently healthy men and women ≥ 60 y old

	Men $(n = 93)$	Student's t-test	Women $(n = 181)$
Hemoglobin (g/l)	152±14 ^a	< 0.0001	140±13
Anemia ($< 130 \text{ g/1 men}; < 120 \text{ g/1 women}$)	5.4%		4.4%
Mean corpuscular volume (fl)	92.3 ± 4.5	< 0.0001	89.6 ± 4.2
Microcytosis (< 80 fl)	1.1%		2.2%
Macrocytosis (> 100 fl)	2.2%		1.1%
Transferrin saturation (%)	36.3 ± 12.9	< 0.004	31.9 ± 10.8
Low (< 16%)	3.3%		3.9%
FEP (μmol/1 rbc)	1.21 ± 0.42	< 0.02	1.37 ± 0.48
High (> 1.77 μ mol/1 rbc)	7.6%		12.8%
Serum ferritin (µg/l)*	$71 (45-112)^{b}$	< 0.0001	54 (29-99)
Insufficient iron stores ($< 12 \mu g/l$)	1.1%		3.3%
Serum copper (µmol/l)	20.4 ± 5.7	< 0.0001	23.8 ± 6.2
Deficient ($< 11.0 \mu\text{mol/l}$)	6.5%		5.1%
Serum retinol (µmol/l)	1.21 ± 0.85	NS	1.38 ± 0.97
Deficient ($< 0.35 \mu\text{mol/l}$)	13.7%		15.9%
Low ($< 0.70 \mu mol/l$)	34.2%		29.0%
Serum folate (nmol/l)	$7(4-13)^{b}$	< 0.008	9(5-17)
Deficient $(<7 \text{ nmol/l})$	50.5%*		33.1
Serum vitamin B_{12} (pmol/l)	$168 (89-320)^{b}$	< 0.0001	240 (111-518)
Deficient (< 74 pmol/l)	6.5%		2.8%
Low (< 148 pmol/l)	$51.1\%^{\dagger}$		30.9%

^aMean \pm s.d. ^bGeometric mean and range \pm 1 s.d. Men vs women: * χ^2 , P < 0.009; † χ^2 , P < 0.003.

Table 4 Hematological and biochemical characteristics of the anemic subjects

				Hemato	logical			Biochemical				Inflammation	
Tests n	Sex	Age (y)	Hb (g/l)	MCV (fl)	FEP (µmol/l rbc)	Sat (%)	SF (μg/l)	Cu (µmol/l)	Folate (nmol/l)	Vitamin B_{12} (pmol/l)	Retinol (µmol/l)	ESR (mm/h)	CRP (mg/dl)
1 ^a	M	78	109	98	1.17	30.0	98	14.6	5	80	2.30	13	1
2^{d}	M	63	116	91	1.75	42.8	72	18.9	11	338	2.55	29	1
3	M	60	121	95	2.99	33.7	62	17.6	4	163	0.59	23	3
4 ^a	M	75	124	102	1.31	32.6	41	21.2	6	398	0.52	8	6
5 ^e	M	68	128	79	2.71	12.3	98	34.4	7	259	_	98	91
6	W	83	82	78	3.43	16.0	9	29.4	10	353	3.35	83	4
7	W	71	87	71	4.50	16.3	33	28.5	10	729	2.20	45	5
8	W	77	90	76	3.54	7.9	5	33.7	7	91	0.49	52	6
$9^{\rm f}$	W	79	103	85	2.02	21.1	35	_	7	170	_	52	38
10	W	77	112	92	1.82	29.9	104	24.3	12	158	1.19	98	19
11	W	74	117	89	1.26	34.3	81	27.1	3	153	0.87	74	17
12	W	63	119	86	1.72	24.8	13	28.9	14	164	1.08	27	3
13 ^a	W	64	119	90	1.13	20.1	59	28.0	7	137	1.57	22	6

^aNeutrophils with 5 or more segmentations. ^bLeukocyte count 11.1×10⁹/l. ^cUrea nitrogen 65 mg/dl. ^dUrea nitrogen 36 mg/dl. ^eAlbumin 3.43 g/l. ^fAlbumin 2.7 g/l. Subject numbers 2, 4, and 12 had low body mass index: 17.3, 16.7 and 16.4 (kg/m²) respectively. Subject numbers 8 and 11 presented increased blood losses in stools: 3.4 and 4.5 ml/day, respectively. A colon neoplasm was diagnosis in subject 8 one month after the study.

Neoplasia, diverticular disease, hiatal hernia and gastric ulcer are the main causes of blood loss. Anemia in the elderly can also be the consequence of a reduction in bone marrow functional reserve (Lipschitz *et al*, 1984), an adaptation to the reduction of the body lean mass with diminished oxygen requirements (Forbes & Halloran, 1976), or due to a reduced erythropoietin secretion (Kario *et al*, 1992).

Elderly subjects living at home have a lower prevalence of anemia than institutionalized older patients (Salive *et al*, 1992). The lower prevalence among free-living elderly may be attributed to a reduced frequency of inflammatory illness and to their high physical activity. The increased physical activity is associated with a higher energy intake with consequent greater food consumption (Fleming *et al*, 1998).

Chronic or acute inflammatory diseases are a wellrecognized cause of a mild to moderate anemia. The reduced erythrocyte production is due to the release of several cytokines by immune activated macrophages, which leads to an inhibition of the erythropoiesis and a block of the iron release from the reticuloendothelial system, with the consequent reduction of iron available for erythropoiesis, and a blunted production of erythropoietin (Lee, 1983; Means & Krantz, 1992). Another mechanism involved in the pathogenesis of anemia is a reduction of erythrocyte survival. The impairment of iron metabolism secondary to inflammation shares many laboratory abnormalities with iron deficiency such as low MCV, serum iron level and transferrin saturation, and increased free erythrocyte protoporphyrin (Lee, 1983; Olivares et al, 1989). However, in contrast to iron deficiency, serum ferritin is increased in inflammatory disease (Lee, 1983; Olivares et al, 1989). Proper diagnosis of iron deficiency is not easy in population groups where inflammation processes are frequent, such as the elderly. However, since serum transferrin receptor concentration is increased in iron deficiency and it is not affected by acute or chronic inflammatory conditions, this measurement is a useful tool in the assessment of iron status in groups with high prevalence of inflammation (Ferguson et al, 1992; Olivares et al, 1995).

The low prevalence of inflammation (11%) and an adequate iron intake may explain the low frequency of

anemia found in our study. Inflammatory processes were the principal etiology of the anemia. In fact, the prevalence of anemia in subjects with inflammation was 22.2% in men and 31.6% in women, while the prevalence was 4.8% and 1.3% in men and women without inflammation, respectively. Average daily iron intake was higher than the 10 mg recommended by the National Academy of Sciences (NRC, 1989). In Chile wheat flour is enriched with 30 mg of iron per 100 g. Other nutrients added to wheat flour are thiamine, riboflavin and niacin.

The USDA composition tables were employed to estimate copper, retinol, folate and vitamin B₁₂ intakes. However it is important to note that these composition tables do not include all foods consumed by the Chilean population. Also, it is well known that geographical variation exits in nutrient content of foods. All these factors may contribute to an underestimate of the intake of these nutrients, which partially explains the high percentage of subjects that have nutrient consumption below the recommended values.

Despite the low dietary intake of all micronutrients, only retinol and folate deficiencies and low vitamin B_{12} levels were of public health significance. Physiological changes that may occur in the aging process (impaired utilization, absorption and storage of nutrients) may explain the high prevalence of deficiency of these nutrients. Iron, copper and vitamin B_{12} deficiencies were an infrequent finding.

The International Vitamin A Consultative Group has recommended that when 15% of the population present low serum retinol levels ($<0.70\,\mu\text{mol/l})$ or 5% have deficient retinol values ($<0.35\,\mu\text{mol/l})$, vitamin A deficiency is a public health problem (Underwood, 1990). In our study 34.2% and 13.7% of the men presented retinol values in the low and deficient ranges, respectively. In women, 29% had low retinol levels and 15.9% deficient values. Thus, vitamin A deficiency is a public health problem among the elderly in Chile.

The high prevalence of folate deficiency found in our elderly subjects (50.5% in men and 33.1% in women) may be explained by a reduced consumption of vegetables and fresh fruits, and by the custom of overcooking foods, which destroys this heat-labile vitamin. We did not study other factors that can affect folate nutrition, such as smoking and chronic alcohol consumption (Ortega *et al*, 1994; Ferro-Luzzi *et al*, 1988). On the other hand, it is possible that



aged subjects have defective folyl polyglutamate absorption. A reduction in gastric acid production is associated with a decreased absorption of folate (Russell *et al.*, 1986).

Many elderly subjects have a decreased gastric production of acid, due to the increase in the prevalence of atrophic gastritis. In this condition there is low vitamin B₁₂ absorption because the protein-bound vitamin is not dissociated and therefore it will not bind to the intrinsic factor. Alternatively the loss of acid can increase stomach and small intestine bacterial overgrowth, which can uptake or bind the vitamin B₁₂ and thus limit vitamin bioavailability (Doscherholmen & Swaim, 1973; Suter et al, 1991). For these reasons, a higher cut-off serum level should be used to detect elderly subjects at an increased risk of developing vitamin $B_{12}\mbox{ deficiency}$ in the elderly. In our study, the frequency of abnormal vitamin B₁₂ serum levels (< 74 pmol/l) was low; however 51.1% of men and 30.9% of women presented low serum levels of this vitamin $(< 148 \, pmol/l)$.

Our aged subjects are likely to have deficiencies of vitamin A, folate and vitamin B₁₂. These vitamin deficiencies increase the health risks of older adults. Vitamin A deficiency may increase the susceptibility of aged subjects to infection (Semba, 1994). On the other hand, deficiencies of folate, vitamin B₁₂ and vitamin B₆ increased the risk of vascular illness through its effects on serum homocysteine levels (Selhub *et al*, 1993). High homocysteine serum values are associated with an increased risk of vascular disease (Graham *et al*, 1997).

Supplementation and food fortification are strategies to prevent mineral and vitamin deficiencies. Fortification of wheat flour with 140 µg of folic acid per 100 g of flour reduces the prevalence of folate and homocysteine abnormal values (Jacques et al, 1999). However, it is important to point out the risk of exclusive folate supplementation or fortification, especially in aged subjects. An excess of folate can mask and/or aggravate a vitamin B₁₂ deficiency, which can precipitate the neurologic damage that accompanies this deficiency. Since a high percentage of our aged subjects have low serum vitamin B₁₂ levels, it seems reasonable to recommend that the supplementation or food fortification must include all deficient vitamins found in this age group. Recently, in our country a national program was began that supplies elderly people of low socioeconomic status with a food fortified with minerals (calcium, phosphorus, magnesium, iron, and zinc) and vitamins (thiamin, riboflavin, folate, vitamins A, B₆, B₁₂ and C).

In conclusion, anemia is not prevalent in free-living elderly subjects when iron intake is adequate. At this age inflammatory process is the main etiology of anemia. This group has an increased risk of developing vitamin A, folate and vitamin B_{12} deficiencies. The elderly should be protected from these deficits by the provision of micronutrient rich foods or by food fortification or supplementation intervention programs.

Acknowledgements—Funded in part by a grant from the Sandoz Foundation for Gerontological Research. The authors thank Ginny Gidi, MPH and Ricardo Uauy, MD PhD for their critical review of this manuscript.

References

DeMaeyer E & Adiels-Tegman M (1985): The prevalence of anaemia in the world. *World Health Stat.* **38**, 302–316.

- Doscherholmen A & Swaim WR (1973): Impaired assimilation of egg ⁵⁷Co vitamin B₁₂ in patients with hypochlorhydria and achlorhydria and after gastric resection. *Gastroenterology* **64**, 913–919.
- Ferguson BJ, Skikne BS, Simpson KN, Baynes RD & Cook JD (1992): Serum transferrin receptor distinguishes the anemia of chronic disease from iron deficiency anemia. *J. Lab. Clin. Med.* **19**, 385–390.
- Ferro-Luzzi A, Mobarhan S, Maiani G, Scaccini C, Sette S, Nicastro A, Ronaldi L, Polito A, Azzini E, Torre SD & Jama MA (1988): Habitual alcohol consumption and nutritional status of the elderly. *Eur. J. Clin. Nutr.* **42**, 5–13.
- Fisher DS & Price DC (1964): A simple serum iron method using the new sensitive chromogen tripiridyl-s-triazine. *Clin. Chem.* 10, 21–30.
- Fleming DJ Jacques PJ, Dallal GE, Tucker KL, Wilson PWF & Wood RJ (1998): Dietary determinants of iron stores in a free-living elderly population: the Framingham heart study. *Am. J. Clin. Nutr.* **67**, 722 733.
- Forbes GB & Halloran E (1976): The adult decline in body lean mass. *Hum. Biol.* **48**, 162–173.
- Graham IM, Daly LE, Refsum HM, Robinson K, Brattström LE, Ueland PM, Palma-Reis RJ, Boers GHJ, Sheahen RG, Israelsson B, Uiterwaal CS, Meleady R, McMaster D, Verhoef P, Witteman J, Rubba P, Bellet H, Wautretch JC, de Valk HW, Salis Luís AC, Parrot-Rouland FM, Tan KS, Higgins I, Garcon D, Medrano MJ, Candito M, Evans A & Andria G. (1997): Plasma homocysteine as a risk factor for vascular disease. The European concerted action project. *J.A.M.A.* 277, 1775–1781.
- INACG (International Anemia Consultative Group) (1985): *Measurement of iron status: a report of the International Anemia Consultative Group.* pp 1–78. Washington, DC: The Nutrition Foundation.
- Jacques PF, Selhub J, Bostom AG, Wilson PWF & Rosenberg IH (1999): The effect of folic acid fortification on plasma folate and total homocysteine concentrations. New Engl. J. Med. 340, 1448–1454.
- Kario K, Matsuo T, Kodama K, Nakao K & Asada R (1992): Reduced erythropoietin secretion in senile anemia. *Am. J. Hematol.* 41, 252–257.
 Lee GR (1983): The anemia of chronic disease. *Semin. Hematol.* 20, 61–80.
 Lipschitz DA, Mitchell CO & Thompson C (1981): The anemia of senescence. *Am. J. Hematol.* 11, 47–54.
- Lipschitz DA, Udupa KB, Milton KY & Thompson CO (1984): Effect of age on hematopoiesis in man. Blood 63, 502-509.
- Mansouri A & Lipschitz DA (1992): Anemia in the elderly patient. *Med. Clin. N. Am.*, **76**, 619–630.
- Means RT Jr & Krantz SB: (1992): Progress in understanding the pathogenesis of the anemia of chronic disease. *Blood* **80**, 1639–1647.
- NRC (National Research Council) (1989): Recommended Dietary Allowances, 10th edn. pp 224–230. Washington, DC: National Academy of Sciences.
- Olivares M, Walter T, Osorio M, Chadud P & Schlesinger L (1989): Anemia of mild viral infection: the measles vaccine as a model. *Pediatrics* **84**, 851–855.
- Olivares M, Walter T, Cook JD & Llaguno S (1995): Effect of acute infection on measurement of iron status: usefulness of the serum transferrin receptor. *Int. J. Pediatr. Hematol. Oncol.* **2**, 31–33.
- Ortega RN, Lopez-Sobaler AM, Gonzalez-Gross MM, Redondo RM, Marzana I, Zamora MJ & Andres P (1994): Influence of smoking on folate intake and blood folate concentrations in a group of elderly Spanish men. *J. Am. Coll. Nutr.* **13**, 68–72.
- Pederneiras A (1996): Consumo de cobre de una población adulta femenina de nivel socioeconómico bajo: contenido real de cobre del agua y de la dieta. Tesis Programa de Magister en Ciencias de la Nutrición, Instituto de Nutrición y Tecnología de los Alimentos (INTA), Santiago de Chile.
- Ríos E, Olivares M, Amar M, Chadud P & Pizarro F & Stekel A (1983): Evaluation of iron status and prevalence of iron deficiency in infants in Chile. In: *Nutrition Intervention Strategies in National Development*. ed. BA Underwood, pp 273–283. New York: Academic Press.
- Russell RM (1992): Changes in gastrointestinal function attributed to aging. Am. J. Clin. Nutr. 55, 1203S-1207S.
- Russell RM, Krasinski SD, Samloff IM, Jacob RA, Hartz SC & Brovender SR (1986): Folic acid malabsorption in atrophic gastritis: possible compensation by bacterial folate synthesis. *Gastroenterology* 91: 1476–1482.
- Salive ME, Cornoni-Huntley J, Guralnick JM, Phillips CL, Wallace RB, Ostfeld AM & Cohen HJ (1992): Anemia and hemoglobin levels in older persons: relationship with age, gender, and health status. J. Am. Geriatr. Soc 40, 489–496.
- Schmidt-Hebbel H, Pennachiotte I & Masson L (1992): *Tabla de Composición Química de Alimentos Chilenos*. Facultad de Ciencias Químicas y Farmaceúticas, Universidad de Chile, Santiago.
- Schwartz S, Dahl J, Ellefson M & Ahlquist D (1983): The hemoquant test: a specific and quantitative determination of heme (hemoglobin) in feces and other materials. *Clin. Chem.* 29, 2061–2067.

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- Selhub J, Jacques PF, Wilson PW, Rush D & Rosenberg IH (1993): Vitamin status and intake as primary determinants of homocysteinemia in an elderly population. *J.A.M.A.* **270**, 2693–2698.
- Semba RD (1994): Vitamin A, immunity, and infection. *Clin. Infect Dis.* **19**, 489–499.
- Suter PM, Golner BB, Goldin BR, Morrow FD & Russell RM (1991): Reversal of protein-bound vitamin B₁₂ malabsorption with antibiotics in atrophic gastritis. *Gastroenterology* **101**, 1039–1045.
- Stander PE (1989): Anemia in the elderly: symptoms, causes, and therapies. *Postgrad. Med.* **85**, 85–96.
- Thompson JN, Erdody P, Brien R & Murray TK (1971): Fluorometric determination of vitamin A in human blood and liver. *Biochem. Med.* 5, 67–89.
- Underwood BA (1990): Methods for the assessment of vitamin A status. J. Nutr. 120, 1459–1463.
- United States Department of Agriculture (1998): USDA Nutrient database standard reference, release 12. United States Department of Agriculture: Riverdale, MD
- Yip R & Dallman PR (1988): The roles of inflammation and iron deficiency as causes of anemia. *Am. J. Clin. Nutr.* **48**, 1295–1300.