

Comparison of the Postprandial Plasma Vitamin A Response in Young and Older Adults

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To assess the influence of age on vitamin A intestinal and liver metabolism in humans, the postprandial plasma concentrations of intestinal-originated vitamin A, i.e., retinyl esters, and liver-originated vitamin A, i.e., retinol, were compared in eight young (20–30 years old) and eight elderly (64–72 years old) healthy men. Plasma and chylomicron retinyl esters and retinol concentrations were measured for up to 24 h following the intake of a test meal that contained 23,300 RE retinyl palmitate. The chylomicron retinyl palmitate response (area under the curve) was not significantly different between the two groups, but its peak was slightly delayed (1 h) in the elderly men. The proportion of the different retinyl esters secreted in the chylomicrons was not significantly different between the two groups. The postprandial plasma retinol concentration did not change in the young participants, whereas it significantly increased in the elderly. These results suggest that vitamin A intestinal absorption and retinol intestinal esterification processes are not markedly modified in the elderly, whereas the chylomicron clearance and the regulation of postprandial plasma retinol concentrations are apparently altered in these subjects.

VITAMIN A is a fat-soluble micronutrient essential for growth, epithelial tissues differentiation, and vision. Thus its metabolism has been extensively studied in animal models and in humans (1,2). Few data are available, however, on the effect of aging on vitamin A metabolism in humans (3), although knowledge of age-related changes in vitamin metabolism is essential for determining vitamin requirements of elderly people.

Studies dedicated to the effect of aging on vitamin A metabolism have reported the following observations: (a) the human plasma retinol concentration remains stable (4–7) or eventually increases (8–10) during aging; (b) the human liver concentration of vitamin A is maintained throughout life (11,12); (c) the intestinal absorption of vitamin A is apparently higher in aged rats than in young rats (13); (d) there is a higher plasma retinyl palmitate response to dietary vitamin A intake in elderly than in young subjects (8,14–15), suggesting an increased vitamin A intestinal absorption in the elderly; (e) no severe vitamin A-deficient status has been detected in healthy, well-nourished elderly subjects. On the whole, these observations suggest that older subjects utilize vitamin A as efficiently as younger ones. However, these data are not sufficient to conclude definitively that older humans have an efficient vitamin A metabolism. Indeed, (a) plasma retinol concentration is a very crude marker of vitamin A status as it is very precisely regulated and only severe deficiency, or hypervitaminosis, can alter it (1,2,16); (b) liver vitamin A stores in the elderly are apparently adequate, but it is not known if the aged human can mobilize liver vitamin A stores as efficiently as the young adult; (c) the slight increase in vitamin A intestinal absorption during aging was

not likely to be significant between adults rats (8 or 17 months old) and aged ones (23 months old) (13,17); (d) the higher plasma retinyl palmitate response in elderly subjects has been attributed to partially impaired chylomicron remnant clearance rather than to increased vitamin A intestinal absorption (15); (e) although it is reasonable to assume that healthy, well-nourished elderly individuals have no severe vitamin A deficiency, a subdeficient status cannot be excluded because such a status is very difficult to assess (18). Thus, additional data are required to enhance our knowledge of the effect of aging on vitamin A metabolism.

As aging affects numerous physiologic processes, it may directly or indirectly affect vitamin A postprandial plasma transport at different levels: (a) it is possible that the age-related alterations of gastrointestinal tract functions (19–22) might modify the efficiency of vitamin A intestinal absorption in older subjects; (b) the age-related modification of enterocyte functions might affect the esterification processes of retinol by impairment of either lecithin-retinol acyltransferase (LRAT) or acyl CoA-retinol acyltransferase (ARAT) (23–25); (c) the plasma transport of retinyl esters from the intestine to the liver is likely affected, as it has been shown that aging delays the clearance of plasma retinyl palmitate (15), but it is not known whether this phenomenon is specific for retinyl palmitate or exists for the other retinyl esters found in the chylomicrons; (d) finally, it is not known if age-related modification of liver cells (26) or extrahepatic cells functions can affect plasma retinol homeostasis in elderly people, but the low efficiency of the relative dose response (RDR) test in elderly peoples (18,27) to detect vitamin A deficiency suggests that this can be the case.

The aim of this study was to enhance our knowledge of the influence of age on vitamin A metabolism by answering the following questions: (a) Does vitamin A intestinal absorption change in elderly people? (b) Is retinol esterification in the enterocyte modified in these people? (c) Is chylomicron retinyl ester metabolism influenced by age? (d) Is postprandial plasma retinol homeostasis impaired in aged subjects? With these aims we compared several steps of the postprandial metabolism of vitamin A in a group of young and a group of elderly healthy subjects.

SUBJECTS AND METHODS

Subjects

Sixteen healthy male volunteers were recruited for this study, eight (20–30 years old) for the young group and eight (64–72 years old) for the elderly group. Informed written consent was obtained from all the volunteers. The protocol was approved by the Medical Ethics Committee of the Regional University Hospital Centers from Clermont-Ferrand and Marseille (France). The subjects had no history of stomach, liver, or pancreatic disease, they were not diabetics, and they had no symptom of lipid malabsorption. They were not taking medications known to affect lipid or vitamin A metabolism or absorption, or vitamin supplements, for at least 6 months. Some characteristics of the subjects are listed in Table 1, along with their fasting plasma vitamin A and lipid values as measured at 7–8 a.m. after a 12-h overnight fast.

Background Diets of the Two Groups

To estimate the composition of the background diets of

the subjects, a 7-day diet diary was completed during the month before the experiment. This diary was analyzed for nutrient composition by using diet analyzer software (GENI, Micro 6, Nancy, France), and data obtained are listed in Table 2. The two groups consumed a typical Western diet with moderate energy consumption. They had a moderate, nonsignificantly different, alcohol consumption: 12.8 ± 7.4 and 21.6 ± 4.1 g/d for the young and elderly groups, respectively. The total vitamin A intake of the two groups was not significantly different. The proportion of vitamin A provided as β -carotene was higher, but nonsignificantly, in the elderly than in the young group ($45.6 \pm 5.9\%$ vs $35.1 \pm 7.5\%$, respectively).

Test meal

The test meal consisted of bread (40 g), wheat semolina (60 g cooked and hydrated with 120 mL water), cooked egg whites (35 g), an oil-in-water emulsion that contained vitamin A, a nonfat yogurt (125 g), and 300 mL of water. The emulsion was incorporated in the semolina just before the intake of the test meal.

The emulsion, prepared by Créalis (Danone Group, Brive, France), was composed of 40 g fat (as sunflower oil containing 69% linoleic acid as quantified by gas-liquid chromatography on a capillary column), 0.4 g of protein, 5.1 g of carbohydrates, 64 mL of water, and $23,253 \pm 849$ RE of vitamin A as retinyl palmitate (Hoffmann-La Roche, Basel, Switzerland). Vitamin A was provided as retinyl palmitate because retinyl esters are the main source of dietary vitamin A in developed countries and, among dietary retinyl esters, retinyl palmitate is the major one.

Table 1. Characteristics of the Subjects*

Subjects	Age (yr)	Body Mass Index (kg/m ²)	Retinol (μ mol/L)	Fasting Plasma Concentration				
				Total Cholesterol (mmol/L)	Esterified Cholesterol (mmol/L)	Free Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triacylglycerol (mmol/L)
Young								
1	28	23.1	1.98	4.46	3.25	1.21	2.76	1.32
2	28	24.7	2.18	5.24	3.95	1.29	2.68	0.88
3	23	21.2	2.03	4.53	3.40	1.13	2.22	0.99
4	20	22.0	3.68	4.73	3.45	1.28	2.54	1.26
5	20	20.6	2.29	4.30	3.30	1.00	2.17	0.81
6	26	23.3	2.24	4.01	3.04	0.97	2.37	1.12
7	30	22.2	2.40	4.27	3.30	0.97	2.11	1.14
8	23	22.7	2.51	4.76	3.60	1.16	2.39	1.41
Mean \pm SEM	24.75 ± 1.35	22.48 ± 0.45	2.41 ± 0.19	4.54 ± 0.13	3.41 ± 0.10	1.13 ± 0.05	2.41 ± 0.08	1.12 ± 0.07
Elderly								
1	65	26.2	2.78	4.35	2.34	2.01	2.51	1.08
2	69	22.8	2.37	4.42	2.19	2.23	2.39	2.32
3	71	22.7	2.05	5.61	3.23	2.38	2.39	1.42
4	66	26.0	2.56	5.14	3.18	1.96	2.39	1.21
5	68	24.3	2.40	4.27	2.27	2.00	2.19	1.25
6	69	31.9	1.91	5.63	3.21	2.42	2.28	2.38
7	72	23.4	2.69	4.82	3.04	1.78	2.38	2.16
8	64	29.4	2.30	6.04	4.12	1.92	2.83	1.82
Mean \pm SEM	68.00 ± 1.00	25.84 ± 1.17	2.39 ± 0.11	5.04 ± 0.24	2.95 ± 0.23	2.09 ± 0.08	2.42 ± 0.07	1.71 ± 0.19
Young versus elderly†		$p < .01$	NS‡	$p < .005$	$p < .05$	$p < .0005$	NS	$p < .01$

*Physical characteristics of the subjects, along with their fasting plasma vitamin A and lipid values as measured after a 12-h overnight fast.

†Significant differences between the young and elderly groups as determined by Student's *t* test for unpaired values.

‡NS, not significant.

Table 2. Composition of the Background Diets of the Two Groups of Subjects*

Daily Intake	Subject Group		Young vs Elderly†
	Young	Elderly	
Energy (KJ)	12,103 ± 1,192	9,343 ± 938	NS
Protein (energy %)	14.3 ± 0.7	17.8 ± 0.7	<i>p</i> < .01
Carbohydrates (energy %)	41.7 ± 2.4	49.7 ± 1.8	<i>p</i> < .05
Fat (energy %)	44.0 ± 2.9	32.6 ± 1.4	<i>p</i> < .005
Retinol (µg)	554.7 ± 142.1	401.6 ± 44.2	NS
β-Carotene (µg)	1,820.4 ± 556.3	2,367.1 ± 566.5	NS
Vitamin A (RE‡)	858.1 ± 155.8	796.1 ± 120.3	NS

*Subjects completed a 7-day diet diary during the month before the experiment. This diary was analyzed for nutrient composition by using diet analyzer software. Values are mean ± SEM.

†The significance of the differences observed between the young and the elderly group were determined by Student's *t* test for unpaired values except for the comparison of retinol intake, which was done using the Mann-Whitney *U* test. NS, not significant.

‡RE, retinol equivalent: 1 RE = 1 µg retinol = 6 µg β-carotene.

The median diameter of the emulsion's lipid droplets was approximately 20 µm as checked by a particle size analyzer (Capa-700, Horiba, Kyoto, Japan).

Study Design

The subjects were asked to avoid vitamin A supplements as well as vitamin A-rich foods the week before the experiments and to have a light meal, depleted of vitamin A, on the evening before the experiments. For that purpose a list of excluded foods was given to the volunteers. After a 12-h overnight fast, at about 7:00 a.m., an antecubital vein was catheterized with an intravenous cannula equipped with disposable obturators (Becton Dickinson, Meylan, France). A baseline fasting blood sample was collected, and the subjects ingested the test meal within 20 min. Foods were ingested in the same succession to avoid variations in gastric emptying or metabolic responses. During the postprandial period the subjects were confined in the human nutrition laboratory, and they did not have physical activity. They were allowed to drink up to 50 mL/h water. Eight hours after the test-meal intake, they had a sandwich depleted of fat and vitamin A. In the evening (at 7:30 p.m.), they had a light meal depleted of fat and vitamin A. Blood samples (10–15 mL) were collected every hour for 5 h and then at 7, 12, and 24 h after the 7:00 a.m. test-meal intake.

Analytical Determinations

Blood was collected in EDTA vacutainers and plasma was prepared immediately by centrifugation (4°C, 10 min, 910 × *g*). The Sf > 1,000 fraction (see Appendix), which contains chylomicrons plus large chylomicron remnants, was isolated from 2 mL plasma layered under 3 mL 0.9% NaCl, by ultracentrifugation at 10°C for 1 h at 24,000 × *g* in a Beckman (Palo Alto, CA) 40.3 rotor (28). Aliquots were frozen and stored at –20°C until analysis, which did not occur more than 3 months after sampling (29). Lipids were determined by enzymatic procedures (30–33) with commercial kits (BioMerieux, Marcy l'Etoile, France). Retinyl es-

ters and retinol were quantified by reverse-phase HPLC on a Kontron AG (Zurich, Switzerland) apparatus with UV detection at 325 nm. The column was a C18-nucleosil (250 × 4.6 mm, 5 µm), and the mobile phase was 100% methanol. Note that this technique efficiently separates retinyl palmitate, retinyl stearate, and retinyl linoleate from each other, but not retinyl oleate from retinyl palmitate. Retinyl laurate, which had been synthesized according to Azais-Braesco et al. (34), was used as internal standard. The quantification was carried out using Kontron MT2 software.

Calculations and Statistical Analysis

The concentrations of the postprandial plasma triacylglycerols and vitamin A (mean ± SEM of eight determinations) are expressed as variations over baseline concentration. The 0–24 h areas under the curves (AUCs) of the postprandial plasma triacylglycerol and vitamin A variations were calculated by the trapezoidal method (28). The Sf < 1,000 retinyl palmitate concentrations were calculated by subtracting the Sf > 1,000 retinyl palmitate concentrations from the whole plasma retinyl palmitate ones.

Two-factor ANOVA (group by time) was used to analyze curves showing patterns of change over time within groups. Analysis of variance (ANOVA) for paired values was used to assess the significance (*p* < .05) of the differences observed between the postprandial and the fasting concentrations in a given group of subjects (35). Student's *t* test for unpaired values (*p* < .05) or the Mann-Whitney *U* test, depending on the distribution of the variables, was used to assess the significance of the differences observed between the two groups of subjects. StatView II software (Abacus, Berkeley, CA) was used for these statistical comparisons.

RESULTS

Fasting Plasma Lipids and Vitamin A Concentrations

As shown in Table 1, fasting plasma total cholesterol, fasting plasma esterified cholesterol, and fasting triacylglycerol concentrations were significantly higher in the elderly group than in the young group, whereas fasting plasma free-cholesterol concentration was significantly lower in the elderly than in the young group. The mean plasma retinol concentrations in the two groups were not significantly different, and no subject had a fasting plasma retinol < 1.4 µmol/L, a threshold assumed to indicate a moderate risk of vitamin A deficiency (10). There were only trace amounts of retinyl palmitate in the fasting plasma of the subjects (data not shown).

Postprandial Chylomicron Triacylglycerols

Figure 1 shows the chylomicron triacylglycerol response to the test meal. For both groups the chylomicron triacylglycerols were significantly higher than baseline from 0 to 12 h after the test meal intake. The chylomicron triacylglycerols peaked 2 h after meal intake in the young group, whereas they peaked 3 h after meal intake in the elderly group. The 1- and 2-h postprandial triacylglycerol concentrations were significantly lower (*p* < .05) in the elderly than in the young. Nevertheless, there was no effect of age on the postprandial triacylglycerol response (0–24

h AUC), that is, 2.16 ± 0.76 (young) versus 1.87 ± 1.0 nmol/L h (elderly).

Postprandial Sf > 1,000 (Chylomicrons) and Sf < 1,000 Retinyl Palmitate

Figure 2 shows the retinyl palmitate responses to the test meal: Figure 2A shows the fraction of retinyl palmitate recovered in the Sf > 1,000 fraction (containing chylomicrons plus large chylomicron remnants), and Figure 2B the fraction of retinyl palmitate recovered in the Sf < 1,000 fraction (containing small chylomicron remnants plus VLDL, LDL, and HDL).

The chylomicron retinyl palmitate concentrations increased after the test-meal intake and remained significantly higher than baseline until 7 h. The curve peaked 3 h after meal intake in the young group, whereas it peaked 4 h after meal intake in the elderly group. The 1- and 2-h postprandial retinyl palmitate concentrations were lower ($p < .05$) in the elderly than in the young, whereas, the 4–7 h retinyl palmitate concentrations were higher ($p < .05$) in the elderly than in the young. The overall chylomicron retinyl palmitate response in the elderly group, that is, 0–24 h AUC, was higher, but nonsignificantly, than the one for the young group, that is, $7,311 \pm 1,049$ versus $4,893 \pm 1,126$ nmol/L h, respectively. In fact, we have calculated that the difference between the mean of the two groups should have been at least $4,200$ nmol/L h in order for these AUCs to be significantly different ($p < .05$) at 80% power. Conversely to what was observed for chylomicron retinyl palmitate, the concentration of retinyl palmitate recovered in the Sf < 1,000 fraction was higher ($p < .05$) in the young than in the elderly at 1, 2, 4, and 5 h (Figure 2B). However, the corresponding AUCs were not significantly different: $11,124 \pm 5,962$ versus $8,348 \pm 5,495$ nmol/L h, but power analysis

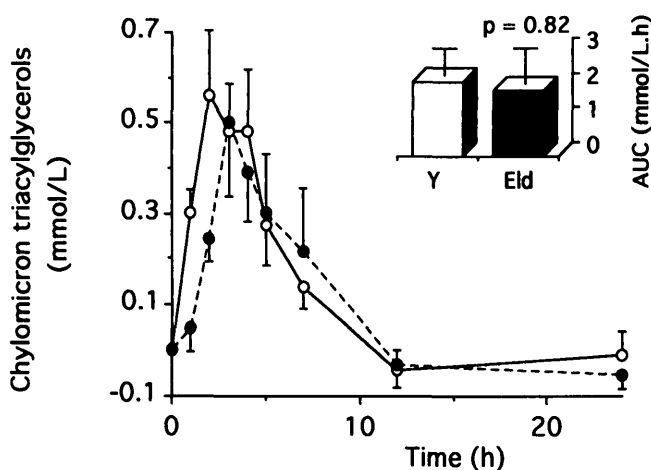


Figure 1. Chylomicron triacylglycerol responses to the test meal in the young (—○—, Y) and the elderly (—●—, Eld) subjects. Values are concentration changes (Δ) from fasting (0 h) values. Points represent the mean \pm SEM of the eight subjects in each group. AUC: area under the curve. Two-factor repeated-measures ANOVA gives a group effect of $p = .64$, a time effect of $p = .0001$, and a group \times time interaction of $p = .4709$. Postprandial concentrations were significantly higher than baseline from 2 to 7 h ($p < .05$, ANOVA for paired values). p: probability value for the AUC comparison.

(80% power) indicated that the difference between the young and the elderly should have been at least $7,650$ nmol/L h in order for these AUCs to be significantly different ($p < .05$).

It is possible that the small number of subjects and the variability in the data explain our failure to find differences between the two groups. Similar considerations may affect other nonsignificant findings in this study.

Postprandial Sf > 1,000 (Chylomicrons) Retinyl Stearate and Retinyl Linoleate

The postprandial chylomicron retinyl stearate and retinyl linoleate responses to the test meal are shown in Figures 3A and 3B, respectively. The concentrations of these retinyl es-

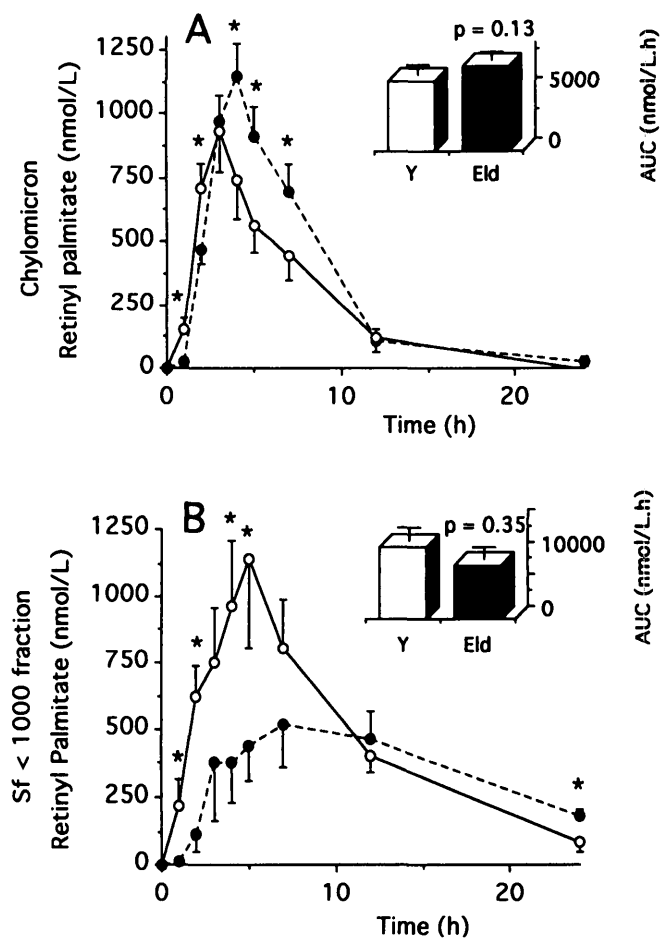


Figure 2. Chylomicron (Sf > 1,000) retinyl palmitate (A) and Sf < 1,000 retinyl palmitate (B) responses in the Young (—○—, Y) and the Elderly (—●—, Eld) subjects. The fraction of retinyl palmitate recovered in the Sf < 1,000 fraction was calculated by subtracting the chylomicron retinyl palmitate to the whole plasma retinyl palmitate. Points represent the mean \pm SEM of the eight subjects in each group. AUC: area under the curve. Two-factor repeated-measures ANOVA gives, for chylomicron retinyl palmitate, a group effect of $p = .0686$, a time effect of $p = .0001$, and a group \times time interaction of $p = .0001$, and for Sf < 1,000 retinyl palmitate a group effect of $p = .085$, a time effect of $p = .0001$, and a group \times time interaction of $p = .0071$. Postprandial concentrations were significantly ($p < .05$, ANOVA for paired values) higher than baseline from 2 to 7 h. \star : Significant difference between the Y and the Eld subjects ($p < .05$, Student's t test for unpaired values). p: probability value for the AUC comparison.

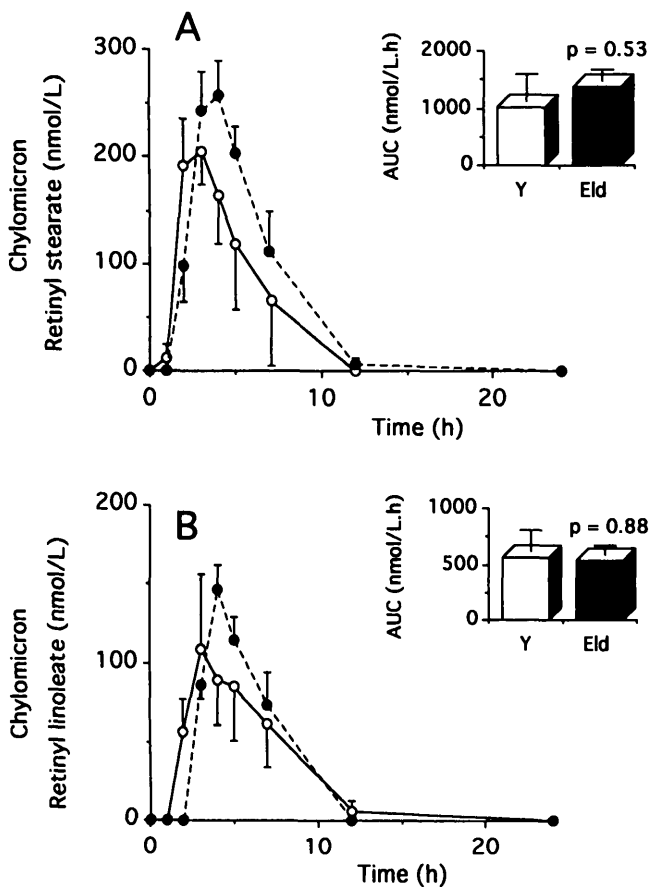


Figure 3. Chylomicron retinyl stearate (A) and chylomicron retinyl linoleate (B) responses to the test meal in the Young (—○—, Y) and the Elderly (—●—, Eld) subjects. Points represent the mean \pm SEM of the eight subjects in each group. AUC: area under the curve. Two-factor repeated-measures ANOVA gives, for chylomicron retinyl stearate, a group effect of $p = .1729$, a time effect of $p = .0001$, and a group \times time interaction of $p = .0001$, and for chylomicron retinyl linoleate a group effect of $p = .648$, a time effect of $p = .0001$, and a group \times time interaction of $p = .0182$. Postprandial chylomicron retinyl stearate concentrations were significantly ($p < .05$, ANOVA for paired values) higher than baseline from 2 to 5 h in the Y subjects and from 3 to 7 h in the Eld subjects. Postprandial chylomicron retinyl linoleate concentrations were significantly ($p < .05$, ANOVA for paired values) higher than baseline from 3 to 7 h in both groups. p: probability value for the AUC comparison.

ters in chylomicron rose after meal intake, peaked at 3 h in the young and at 4 h in the elderly, and decreased to reach the baseline value at 12 h. As previously described for retinyl palmitate, the 5- and 7-h retinyl stearate and retinyl linoleate concentrations tended to be higher, yet not significantly, in the elderly than in the young. The elderly group's retinyl stearate AUC was slightly, yet not significantly, higher than the young group's: $1,357 \pm 192$ (elderly group) versus $1,018 \pm 463$ (young group) nmol/L h, whereas the two groups' retinyl linoleate AUCs were similar, that is, 563 ± 194 (young group) versus 531 ± 84 (elderly group) nmol/L h.

Postprandial Plasma Retinol

The plasma retinol response to the test meal is shown in Figure 4. It is noteworthy to observe the striking difference between the plasma retinol response (AUC) in the young

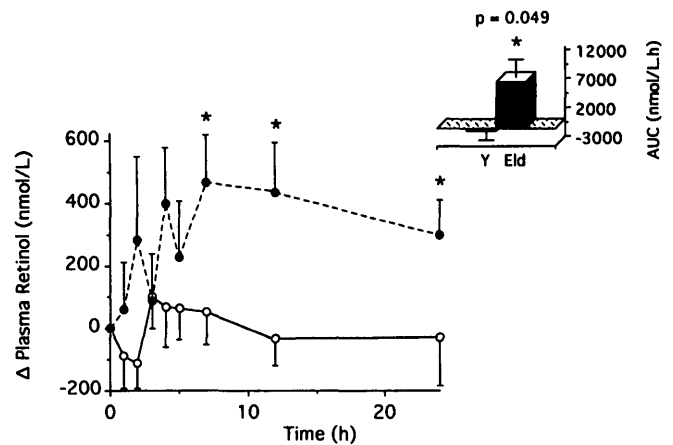


Figure 4. Plasma retinol response to the test meal in the Young (—○—, Y) and the Elderly (—●—, Eld) subjects. Values are concentration changes (Δ) from fasting (0 h) values. Points represent the mean \pm SEM of the eight subjects in each group. AUC: area under the curve. Two-factor repeated-measures ANOVA gives a group effect of $p = .0065$, a time effect of $p = .0152$, and a group \times time interaction of $p = .3014$. \star : Significant difference between the Y and the Eld subjects ($p < .05$, Student's t test for unpaired values). p: probability value for the AUC comparison.

and in the elderly. In fact, the plasma 0–24 h retinol AUC was significantly higher in the elderly ($8,310 \pm 3,074$ nmol/L h) than in the young ($-147 \pm 2,465$ nmol/L h). Nevertheless, the absence of a significant interaction between group and time makes this apparent difference hard to interpret. If there were truly a change toward greater differences at later times, one would expect the interaction to be significant. As suggested above, the small number of subjects and the variability in the data probably explain our failure to find clear differences between the two groups.

DISCUSSION

The postprandial plasma retinol palmitate response suggests that preformed vitamin A intestinal absorption is not markedly affected in aged subjects.—The influence of age on the efficiency of intestinal absorption of triacylglycerols and preformed vitamin A was estimated by comparing the chylomicron triacylglycerols and retinyl esters responses (AUCs) obtained in both groups of subjects. Although this methodology does not provide a direct measurement of the efficiency of vitamin A intestinal absorption, it has been used successfully to compare vitamin A intestinal absorption efficiency in humans (14,15,36).

As the overall chylomicron triacylglycerol and retinyl palmitate AUCs were not significantly different between the young and the elderly subjects, we conclude that the intestinal enzymes involved in the intestinal absorption of triacylglycerols and retinyl palmitate (37–38) were not sufficiently affected in older subjects, if they are, to lead to a substantial modification of the intestinal absorption of these molecules. This result is consistent with previous results obtained in adult rats (13,17).

The lower chylomicron triacylglycerol and retinyl ester concentrations at 1 and 2 h after meal intake in the elderly suggest that the appearance of lipids and vitamin A in the

chylomicrons was slightly delayed in these subjects. This may result from a lower gastric emptying rate in elderly as compared to young people (19) or from a slower assembly rate of chylomicrons in the elderly's enterocytes.

The proportion of the different retinyl esters recovered in the chylomicrons suggests that retinol esterification is not markedly affected in elderly subjects.—The esterification process of retinol in the enterocyte is well elucidated (1,2,23,25,39). Nevertheless, to our knowledge no data are available concerning its efficiency in older humans. Because measuring this process requires intestinal mucosa biopsy that could not have been performed in our healthy subjects, we attempted to evaluate it indirectly by comparing the pattern of retinyl esters recovered in the chylomicron fraction following a linoleic acid-rich test meal. Indeed, we hypothesize that a modification of the relative activity of the two enzymes involved in retinol esterification, i.e., LRAT (40) and ARAT (41), can affect the proportion of retinyl linoleate to retinyl palmitate and stearate recovered in the chylomicrons. As we did not find any significant difference between the chylomicron retinyl ester pattern recovered in the young and the elderly subjects, we suggest that the biochemical pathways involved in the esterification process of retinol in the enterocyte were not markedly affected in the older subjects.

As our data provide only indirect evidence, additional studies are required to draw definitive conclusions about the retinol esterification processes in aged humans.

The postprandial transport of vitamin A from the intestine to the liver is delayed in the older subjects.—The delayed chylomicron retinyl palmitate response observed in the elderly is in agreement with a previous observation (15) and has been attributed to a delayed chylomicron clearance in these subjects. This phenomenon can result from a diminished endothelial lipoprotein lipase (LPL) lipolytic activity as well as from an impaired removal of the small chylomicron remnants by their receptors. The first hypothesis seems the most likely, since several studies have clearly shown that, in humans, LPL activity decreases with increasing age (42–47), while one study failed to establish a clear relationship between aging and chylomicron remnant receptor activity (45).

In the postprandial period, retinyl palmitate is a useful marker of chylomicrons and their remnants (46–48), so it is likely that retinyl palmitate recovered in the Sf < 1,000 fraction was transported mostly by small chylomicron remnants. Consequently, comparing the proportion of retinyl palmitate recovered in the Sf > 1,000 (chylomicrons and large chylomicron remnants) fraction and in the Sf < 1,000 fraction allows us to estimate the efficiency of conversion of large chylomicron remnants to small chylomicron remnants, and thus allows us to evaluate the efficiency of LPL lipolysis in both subject groups. The results obtained, i.e., the higher proportion of retinyl palmitate in the chylomicron fraction concomitant with the lower proportion of retinyl palmitate in the Sf < 1,000 fraction in the elderly as compared to the young, argue for a slower lipolysis of chylomicrons by LPL in the elderly, and thus confirm previous findings (42–44,48).

The fact that the delay observed for retinyl palmitate in the elderly was also observed for the other retinyl esters allows us to conclude that this phenomenon was not specific for retinyl palmitate, and thus supports the hypothesis that the delayed retinyl palmitate clearance was the consequence of an impaired clearance of chylomicron particles rather than the consequence of a specific metabolism of retinyl palmitate.

The regulation of plasma retinol concentrations during the postprandial period is possibly altered in older subjects.—As was found in several previous studies (4–7), the fasting plasma retinol concentration was not significantly different between the young and the elderly subjects. This was expected, because the subjects were healthy and well nourished. Nevertheless, the higher postprandial plasma retinol response in the elderly subjects was unexpected. In fact, it was due mainly to the retinol concentrations measured from 7 to 24 h after meal intake and, in agreement with a previous result (8), there was no significant difference in the plasma retinol response of the two groups for 1 to 5 h.

Such a postprandial plasma retinol increase is usually observed in vitamin A-deficient subjects after a vitamin A load in the RDR test, one of the most accurate means to assess vitamin A status (49). Thus the response obtained in the elderly brings into question the vitamin A status of the elderly enrolled in this study. However, these subjects certainly did not have a severe vitamin A-deficient status as assessed by clinical observations, the fasting plasma retinol concentrations, and the diet diaries.

A first explanation of this peculiar response could be that these subjects had a subdeficient status rather than a deficient status; indeed the markers of deficient status are not very sensitive to a subdeficient one. As the diet diaries analysis showed that β -carotene accounted for about 50% of dietary vitamin A, one can suggest that this status might result from a lower provitaminic A activity of β -carotene in these subjects. This lower provitaminic A activity could result from an age-related diminished absorption of β -carotene or an age-related diminished activity of β -carotene dioxygenase. However, this hypothesis seems unlikely, since a study by Rasmussen et al. (50) has shown higher retinyl esters responses in elderly than in young subjects following the ingestion of mixed carotenoid-vitamin A meals.

A second hypothesis could be that the liver vitamin A stores were not as easily mobilized in the elderly as in the young because of possible age-related modifications of hepatocyte functions (26). Indeed, an impaired transfer of vitamin A from liver stellate cells, where it is stored, to hepatocytes, where it associates with RBP, may have led, as in vitamin A-deficient subjects, to an abnormally high concentration of free RBP in hepatocytes, which in turn may have led to a higher secretion of RBP-retinol in the plasma following the vitamin A load.

A third hypothesis could be that an impaired uptake of plasma RBP-retinol by extrahepatic tissues might have led to a transient increase of plasma retinol.

Whatever the mechanism involved, it is tempting to suggest that this "abnormal" postprandial plasma retinol response is related to the higher fasting plasma retinol concentrations

that have been observed in elderly as compared to young subjects in several studies (8–10). Furthermore, this phenomenon might partly explain why the RDR test is not as reliable in elderly as in young people to detect vitamin A deficiency (27).

In conclusion, our results suggest that preformed vitamin A absorption, esterification processes of retinol, and retinyl ester secretion in the chylomicrons are not markedly affected in older subjects, whereas the plasma transport of retinyl esters and the regulation of plasma retinol concentration during the postprandial period are possibly altered in these subjects. Nevertheless, the variability of the responses obtained and the small number of subjects enrolled in this study may have prevented us from finding some genuine differences, and a study with more subjects should be performed to confirm the results obtained.

ACKNOWLEDGMENTS

This work was supported in part by Crealis-groupe Danone and the French Ministry of Research (grant #93/4930 from INRA-AIP "Nutriage"). The authors wish to thank L. Morin and M. Genest for their help in blood collection and chylomicron preparation, respectively, E. Verdier for the analysis of the diet diaries, and E. Albuissou for her statistical advice.

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Received March 26, 1996

Accepted September 3, 1997

Appendix

Sf is the flotation rate coefficient of lipoproteins. It is expressed in Svedberg units for density salt solution of 1.063 g/mL. An Sf > 1,000 value corresponds to particles of $d < 0.96$ g/mL.