Dietary nutrient intakes and skin-aging appearance among middle-aged American women[1−4]

Maeve C Cosgrove, Oscar H Franco, Stewart P Granger, Peter G Murray, and Andrew E Mayes

ABSTRACT

Background: Nutritional factors play a key role in normal dermatologic functioning. However, little is known about the effects of diet on skin-aging appearance.

Objective: We evaluated the associations between nutrient intakes and skin-aging appearance.

Design: Using data from the first National Health and Nutrition Examination Survey, we examined associations between nutrient intakes and skin aging in 4025 women (40–74 y). Nutrients were estimated from a 24-h recall. Clinical examinations of the skin were conducted by dermatologists. Skin-aging appearance was defined as having a wrinkled appearance, senile dryness, and skin atrophy.

Results: Higher vitamin C intakes were associated with a lower likelihood of a wrinkled appearance [odds ratio (OR) 0.89; 95% CI: 0.82, 0.96] and senile dryness (OR: 0.93; 95% CI: 0.87, 0.99). Higher linoleic acid intakes were associated with a lower likelihood of senile dryness (OR: 0.75; 95% CI: 0.64, 0.88) and skin atrophy (OR: 0.78; 95% CI 0.65, 0.95). A 17-g increase in fat and a 50-g increase in carbohydrate intakes increased the likelihood of a wrinkled appearance (OR: 1.28 and 1.36, respectively) and skin atrophy (OR: 1.37 and 1.33, respectively). These associations were independent of age, race, education, sunlight exposure, income, menopausal status, body mass index, supplement use, physical activity, and energy intake.

Conclusions: Higher intakes of vitamin C and linoleic acid and lower intakes of fats and carbohydrates are associated with better skin-aging appearance. Promoting healthy dietary behaviors may have additional benefit for skin appearance in addition to other health outcomes in the population.   *Am J Clin Nutr* 2007;86:1225–31.

INTRODUCTION

Skin aging is a continuous process that is heavily determined by the combined influences arising from intrinsic aging, the environment (eg, sun exposure), and lifestyle factors [eg, cigarette smoking, low body mass index (BMI; in kg/m^2), and menopausal status] (1–5). Among these factors, the harmful effects of chronic sun exposure (photoaging) and smoking on premature skin aging are widely supported (6–9). During the course of skin aging, both skin function and appearance are affected. Changes in appearance are the most visible signs of aging and include wrinkles, irregular pigmentation, sagging, atrophy, elastosis, and telangiectasia (1, 6). Such changes in appearance have substantial negative affects on self-esteem and social well-being (10).

Furthermore, appearance was shown to be an indicator of overall health status, and it has been shown that "looking old for one's age" is associated with increased risk of mortality (11, 12).

Balanced nutrition is essential not only to prevent chronic disease such as cardiovascular disease, certain cancers, and diabetes (13) but also to maintain health and ensure normal functioning. Certain nutrients were identified to play a critical role in the normal functioning of the skin, particularly when nutrient deficiencies are apparent, eg, vitamin C in collagen synthesis (14, 15). Several studies have observed improved protection of the skin against sun damage (photoprotection) by dietary supplementation with vitamins E and C, carotenoids (β-carotene and lycopene), and polyunsaturated fatty acids (PUFAs) (16, 17). However, those studies are limited by the use of supplements, some with several active ingredients, making it difficult to determine which nutrient is having an effect. One study observed a photoprotective effect of a diet higher in vegetables, fruit, and olive oil on the skin (18). Whether habitual dietary intakes have a significant effect on skin-aging appearance has not been shown. This is critical to adequately design potential interventions targeted to improve or delay the skin-aging process. Therefore, in the present cross-sectional analysis, using the first National Health and Nutrition Examination Survey (NHANES I) (19), we examined the relation between nutrient intakes and the prevalence of the appearance of wrinkles, senile dryness (dryness as a result of aging), and skin atrophy (thinning) in middle-aged women. This examination allowed us to examine the relation between nutrient intakes, rather than supplements, and skin-aging appearance, rather than photoprotection, for the first time to our knowledge.

SUBJECTS AND METHODS

Data source

The NHANES I was conducted in the United States by the National Center for Health Statistics between 1971 and 1974

(19). Briefly, NHANES I was conducted on a nationwide sample of ≈32 000 noninstitutionalized persons aged 1–74 y. Details of methods, including the development, plan, and operation of the survey and data collection forms have been published and are available elsewhere (20–22).

Study sample

All women aged ≥ 40 y were eligible for inclusion. From the original available sample of 23 808 subjects, 10 152 men, 8477 women aged < 40 y, 1062 women who did not have a dermatologic examination, and 92 women with unsatisfactory 24-h dietary recalls were excluded. The final sample consisted of 4025 women aged 40–74 y.

Assessment of skin aging

A complete clinical dermatologic examination of the skin was undertaken to evaluate variations in texture and color, certain manifestations of aging, and all pathologic changes. The dermatologic examinations were performed by 101 dermatologists that followed a studywide protocol after uniform training and standardized definitions (23). To ensure consistency with the examination protocol, a random sample of the 20 637 examinations was checked by a senior dermatologist (24). The dermatologist classified the subjects into 1 of 3 categories of cumulative lifetime sunlight exposure: *1*) low (unimpressive), *2*) moderate, and *3*) high (considerable), based on the subjects' occupation and amount of leisure time spent outdoors. Skin aging was defined by 3 independent determinants of the process: wrinkled appearance, senile dryness (dryness as a result of aging), and skin atrophy (thinning).

Dietary assessment

A 24-h dietary recall was administered to each respondent by a trained dietary interviewer, with 3-dimensional food models, including household measures, to estimate food portions (23). The interviewer probed for clarity of foods and beverages consumed and for commonly forgotten items (eg, sugar in tea, beverages with meals). Estimates of nutrient intake for each food and beverage reported were obtained from the US Department of Agriculture food composition data (25).

Assessment of other variables

Height and weight were measured using standard methods (26), and BMI was calculated. The physical activity question about nonrecreational activity was: "In your usual day, aside from recreation, how active are you?" The possible responses were *1*) very active, *2*) moderately active, or *3*) quite inactive. Additional covariate information about age, smoking habits, menopausal status, race, education, and family income was obtained with the use of questionnaires.

Statistical analyses

We first conducted univariate analyses to describe the distribution of nutrient intakes and demographic and lifestyle attributes by having a wrinkled appearance, senile dryness, and skin atrophy. Significant differences were assessed using Pearson's chi-square and independent *t* tests for categorical and continuous variables, respectively. Differences in mean nutrient intakes were assessed with the use of analysis of variance, adjusting for age (continuous), race (white, black, other),

energy intake (continuous), education [<12 y, high school graduation (12 y), >12 y], sunlight exposure (unimpressive, moderate, considerable), total family income (<$5000, $5000–9999; ≥$10 000), menopausal status (responded yes to the question "Have your menstrual periods stopped entirely?" compared with no), BMI (continuous), supplement use (responded yes to the question "Are you taking vitamins or minerals?" compared with no), and self-reported daily physical activity (very active, moderately active, quite inactive). Intakes of linoleic acid, total dietary cholesterol, calcium, and vitamins A and C were log transformed, because they were not normally distributed.

To determine the associations of nutrient intakes with skin-aging appearance, nutrients that substantially changed the effect on the outcomes ($P < 0.2$) were examined with the use of binary logistic regression analysis (27). We used logistic regression models in 3808 women with complete data, controlling for age, race, energy intake, education, sunlight exposure, family income, menopausal status, BMI, supplement use, and physical activity to determine the associations of fat, carbohydrate, thiamine, and vitamin C with a wrinkled appearance; of saturated fatty acids, oleic acid, linoleic acid, and vitamin C with senile dryness; and of fat, carbohydrate, and linoleic acid with skin atrophy. Variables that substantially changed the effect on the outcomes examined ($P < 0.2$) (27) or were associated with skin aging in prior studies (3–5, 22) were considered as potential confounders. Family income may be related to skin-aging appearance thorough pathways other than its influence on diet; therefore, it was included in all models. The odds ratio (OR) represents the odds for a 1-unit increment (eg, 1 g protein). To illustrate nutritionally relevant estimates, new ORs were calculated on the basis of 33% of the median intake for each nutrient (except for log-transformed nutrients and thiamine, whose median intake was < 1 mg) (28).

Subgroup analysis

Cigarette smoking is a well-established independent risk factor for facial wrinkling and skin aging (6–9). In this analysis, smoking data were only collected for 1401 women ($n = 539$ current and previous smokers; $n = 862$ never smoked). Therefore, stratified analysis was conducted to examine skin-aging appearance without ignoring the smoking data or losing large sample numbers because of the missing data.

We used a *P* value < 0.05 for significance, and all tests were 2-sided. All analyses were performed with SPSS, version 14 (SPSS Inc, Chicago, IL).

RESULTS

Characteristics of the study sample

A wrinkled appearance was present in 899 (22.3%), senile dryness in 1159 (28.8%), and skin atrophy in 515 (12.8%) women. The distribution of the skin-aging appearance in the 4025 women is shown by the presence or absence of wrinkles, senile dryness, and skin atrophy in **Figure 1**. Of the 3 signs of skin-aging appearance, wrinkles were significantly correlated with senile dryness ($r = 0.36$) and skin atrophy ($r = 0.52$). Senile dryness was significantly correlated with skin atrophy ($r = 0.30$). Characteristics of all women and of each outcome separately are shown in **Table 1**. Skin-aging outcomes were found significantly
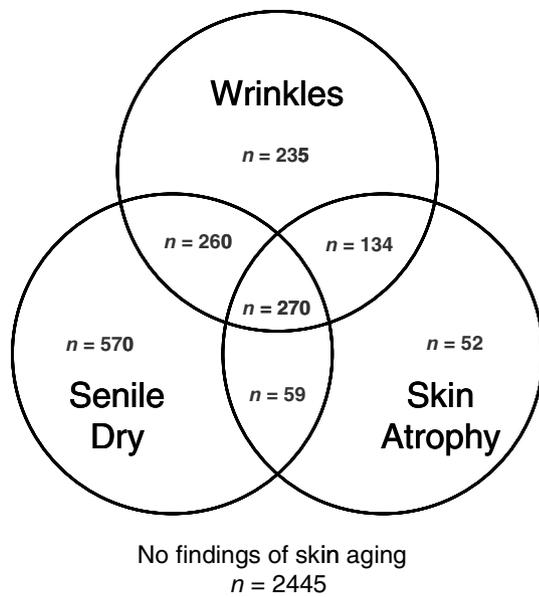
FIGURE 1. Distribution of 4025 women by the presence of a wrinkled appearance, senile dryness, and skin atrophy.

in older women; women with a wrinkled appearance, senile dryness, and skin atrophy were $\approx$10 y, 10 y, and 9 y older, respectively. Women with the appearance of wrinkles, with senile dryness, and with skin atrophy were more likely to be white, have <12 y education, have a low family income, be postmenopausal, and have higher sunlight exposure. Women with skin atrophy were significantly associated with a lower BMI, and women with a wrinkled appearance and with senile dryness were less likely to be physically active. No significant differences in supplement users and skin-aging outcomes were observed.

Distribution of nutrient intakes by skin-aging appearance

Multivariate-adjusted means for nutrient intakes (adjusted for age, race, energy intake, education, sunlight exposure, family income, menopausal status, BMI, supplement use, and physical activity) are shown by outcomes of skin-aging appearance in **Table 2**. Women with a wrinkled appearance had significantly lower intakes of protein, total dietary cholesterol, phosphorus, potassium, vitamin A, and vitamin C than did women without a wrinkled appearance. Women with senile dry skin had significantly lower intakes of linoleic acid and vitamin C than did women without senile dry skin. Women with skin atrophy had a

TABLE 1
Demographic, lifestyle, and dietary characteristics of women aged 40–74 y in the first National Health and Nutrition Examination Survey (NHANES I) by the appearance of skin aging

Variables	All women ($n = 4025$)	Wrinkled appearance			Senile dryness			Skin atrophy		
		Absence ($n = 3126$)	Presence ($n = 899$)	P^1	Absence ($n = 2866$)	Presence ($n = 1159$)	P^1	Absence ($n = 3510$)	Presence ($n = 515$)	P^1
Age (y)	58.1 ± 11.2^2	55.9 ± 11.1	65.6 ± 7.5	< 0.001	55.3 ± 11.1	65.0 ± 7.9	< 0.001	56.9 ± 1.2	66.1 ± 7.5	< 0.001
BMI (kg/m²)	26.4 ± 5.6	26.5 ± 5.7	26.2 ± 5.5	NS	26.4 ± 5.7	26.4 ± 5.4	NS	26.5 ± 5.7	25.9 ± 5.3	0.020
Energy (kcal)	1376 ± 559	1397 ± 571	1305 ± 508	< 0.001	1403 ± 568	1310 ± 529	< 0.001	1389 ± 567	1289 ± 487	< 0.001
Race (%)				< 0.001			0.003			< 0.001
White	82.2	79.3	92.0		80.9	85.2		80.7	92.4	
Black	17.1	19.8	7.8		18.2	14.4		18.6	7.2	
Other	0.7	0.8	0.2		0.8	0.3		0.7	0.4	
Education (%)[3]				< 0.001			< 0.001			< 0.001
<12 y	54.8	52.0	64.5		51.0	64.3		53.1	66.3	
12 y	29.4	31.7	21.1		32.5	21.5		30.8	19.7	
>12 y	15.9	16.3	14.4		16.5	14.2		16.1	14.0	
Family income (%)[4]				< 0.001			< 0.001			< 0.001
<$5000	41.7	38.4	52.9		36.3	54.9		39.7	55.0	
$5000–9999	29.5	29.7	28.9		30.7	26.6		29.9	27.0	
>$10 000	28.8	31.8	18.2		32.9	18.5		30.4	17.9	
Physical activity (%)				0.009			< 0.001			NS
Quite inactive	11.9	12.3	10.5		10.5	15.1		11.9	11.5	
Moderately active	49.8	48.5	54.3		48.5	53.1		49.2	54.2	
Very active	38.3	39.2	35.3		41.0	31.8		38.9	34.4	
Postmenopausal (%)[5]	75.5	69.9	95.0	< 0.001	67.8	94.5	< 0.001	72.7	94.8	< 0.001
Sunlight exposure (%)[6]				< 0.001			< 0.001			< 0.001
Low	45.9	47.0	42.1		47.7	41.4		47.1	37.4	
Medium	39.0	39.0	38.8		38.9	39.1		38.2	43.8	
High	15.2	14.0	19.1		13.4	19.5		14.6	18.8	
Supplement use (%)	37.0	36.9	37.6	NS	37.8	35.0	NS	37.2	35.7	NS

[1] Independent t test was used for continuous variables, and chi-square test was used for categorical variables.
[2] $\bar{x} \pm$ SD (all such values).
[3] $n = 3993$.
[4] $n = 3852$.
[5] $n = 3036$.
[6] $n = 4004$.

TABLE 2
Nutrient intakes in women by the appearance of skin aging[1]

	Wrinkled appearance			Senile dryness			Skin atrophy		
Nutrients	Absence (*n* = 2925)	Presence (*n* = 856)	*P*[2]	Absence (*n* = 2705)	Presence (*n* = 1103)	*P*[2]	Absence (*n* = 3322)	Presence (*n* = 486)	*P*[2]
Protein (g/d)	57.2 ± 0.34[3]	54.8 ± 0.66	0.002	57.0 ± 0.36	55.9 ± 0.59	0.124	56.8 ± 0.32	55.4 ± 0.86	0.115
Fat (g/d)	55.5 ± 0.27	55.9 ± 0.52	0.486	55.5 ± 0.28	55.7 ± 0.46	0.798	55.5 ± 0.25	55.8 ± 0.67	0.691
Carbohydrate (g/d)	158 ± 0.78	160 ± 1.51	0.153	158 ± 0.82	159 ± 1.34	0.677	158 ± 0.72	160 ± 1.96	0.253
Saturated fatty acid (mg/d)	19.9 ± 0.13	19.9 ± 0.26	0.853	19.9 ± 0.14	19.9 ± 0.23	0.807	19.9 ± 0.12	19.9 ± 0.34	0.936
Oleic acid (mg/d)	21.4 ± 0.13	21.5 ± 0.25	0.765	21.4 ± 0.13	21.7 ± 0.22	0.205	21.5 ± 0.12	21.3 ± 0.32	0.543
Linoleic acid (g/d)[4]	1.73 ± 0.01	1.72 ± 0.02	0.655	1.74 ± 0.01	1.68 ± 0.02	0.008	1.73 ± 0.01	1.68 ± 0.03	0.049
Dietary cholesterol (mg/d)[4]	5.41 ± 0.01	5.33 ± 0.03	0.014	5.40 ± 0.01	5.38 ± 0.02	0.641	5.40 ± 0.01	5.37 ± 0.04	0.484
Calcium (mg/d)[4]	6.12 ± 0.01	6.10 ± 0.02	0.536	6.13 ± 0.01	6.09 ± 0.02	0.108	6.11 ± 0.01	6.15 ± 0.03	0.220
Phosphorus (mg/d)	880 ± 5.02	858 ± 9.75	0.046	879 ± 5.29	867 ± 8.61	0.244	875 ± 4.67	877 ± 12.66	0.862
Iron (mg/d)	9.40 ± 0.06	9.22 ± 0.12	0.186	9.35 ± 0.07	9.38 ± 0.11	0.853	9.38 ± 0.06	9.22 ± 0.16	0.356
Sodium (mg/d)	1615 ± 14.9	1633 ± 29.0	0.590	1628 ± 15.7	1597 ± 25.6	0.329	1610 ± 13.9	1681 ± 37.6	0.081
Potassium (mg/d)	1826 ± 11.8	1771 ± 23.0	0.036	1827 ± 12.5	1782 ± 20.3	0.067	1813 ± 11.0	1817 ± 29.9	0.901
Vitamin A (IU/d)[4]	7.98 ± 0.02	7.88 ± 0.04	0.021	7.98 ± 0.02	7.90 ± 0.03	0.061	7.96 ± 0.02	7.96 ± 0.05	0.995
Thiamine (mg/d)	0.81 ± 0.01	0.83 ± 0.01	0.162	0.81 ± 0.01	0.81 ± 0.01	0.825	0.81 ± 0.01	0.83 ± 0.02	0.343
Riboflavin (mg/d)	1.23 ± 0.01	1.21 ± 0.02	0.448	1.23 ± 0.01	1.21 ± 0.02	0.501	1.22 ± 0.01	1.24 ± 0.03	0.654
Niacin (mg/d)	13.1 ± 0.11	12.8 ± 0.22	0.128	13.1 ± 0.12	13.0 ± 0.19	0.546	13.1 ± 0.10	12.8 ± 0.28	0.278
Vitamin C (mg/d)[4]	3.94 ± 0.02	3.82 ± 0.04	0.015	3.95 ± 0.02	3.83 ± 0.04	0.009	3.92 ± 0.02	3.86 ± 0.05	0.282

[1] Adjusted for age, race, energy intake, education, sunlight exposure, family income, menopausal status, BMI, supplement use, and physical activity.
[2] Derived from ANOVA.
[3] $\bar{x}$ ± SE (all such values).
[4] Log transformed.

significantly lower linoleic acid intake than did women without skin atrophy.

Logistic regression analysis of nutrient intake and skin-aging appearance

Multivariate-adjusted logistic regression ORs for skin-aging appearance outcomes with selected nutrient intakes are shown in **Table 3**. A 1-unit increase on the log scale in intakes of vitamin

TABLE 3
Multivariate-adjusted odds ratios (ORs) relating nutrient intake to skin aging appearance[1]

	Increment[2]	OR (95% CI)	*P*
Wrinkled appearance			
Fat (g/d)	16.73	1.28 (1.08, 1.53)	0.005
Carbohydrate (g/d)	49.15	1.36 (1.14, 1.63)	0.001
Thiamine (mg/d)	1.00	1.31 (1.05, 1.63)	0.019
Vitamin C (mg/d)[3]	1.00	0.89 (0.82, 0.96)	0.003
Senile dryness			
Saturated fatty acid (mg/d)	5.80	0.90 (0.81, 0.99)	0.030
Oleic acid (mg/d)	6.41	1.18 (1.05, 1.33)	0.006
Linoleic acid (g/d)[3]	1.00	0.75 (064, 0.88)	< 0.001
Vitamin C (mg/d)[3]	1.00	0.93 (0.87, 0.99)	0.034
Skin atrophy			
Fat (g/d)	16.73	1.37 (1.09, 1.71)	0.006
Carbohydrate (g/d)	49.15	1.33 (1.06, 1.66)	0.012
Linoleic acid (g/d)[3]	1.00	0.78 (0.65, 0.95)	0.012

[1] Model adjusted for age, energy intake, race, menopausal status, sunlight exposure, BMI, family income, education, supplement use, and physical activity. For each outcome the nutrient intakes in the model were adjusted for each other.
[2] Based on a 1-unit increment for log-adjusted nutrients and thiamine and based on an increase in 33% of the median intake for all other nutrients.
[3] Log transformed.

C were associated with an 11% reduction in the odds of a wrinkled appearance and a 7% reduction in the odds of senile dryness. Similarly, a 1-unit increase on the log scale in intakes of linoleic acid were associated with 25% and 22% reductions in the odds of senile dryness and skin atrophy, respectively. A 17-g increase in fat and a 50-g increase in carbohydrate intakes increased the ORs of a wrinkled appearance and skin atrophy. The multivariate-adjusted logistic regression models yielded an R^2 of 0.17, 0.16, and 0.15 for a wrinkled appearance, senile dryness, and skin atrophy, respectively. Variables that substantially affected the regression coefficients in the models were age, race, and sunlight exposure for all outcomes, plus menopausal status for wrinkles and senile dryness and BMI for skin atrophy. Supplement use was not significantly associated with any of the 3 signs of skin-aging appearance; no interactions were observed between mean nutrient intakes and supplement use (data not shown).

Subgroup analysis

In NHANES I, smoking data were collected for a subsample of adults. In this study smoking information was available for only 1401 women, of which 539 (38%) were smokers (current and previous) and 862 (62%) had never smoked. The mean age of smokers was 54.5 y; the mean age of nonsmokers was 58.5 y (*P* < 0.001). In this subgroup the majority of the associations observed between nutrients and skin-aging appearance in the total population remained after the stratification for smoking. Furthermore, additional associations were observed among smokers. Smokers with a wrinkled appearance had significantly lower intakes of protein and niacin than did smokers without wrinkled appearance (*P* < 0.05), and smokers with skin atrophy had higher calcium intakes than did smokers without skin atrophy (*P* < 0.05) (data not shown).

DISCUSSION

We found that higher intakes of vitamin C and linoleic acid and lower intakes of fats and carbohydrates were associated with better skin-aging appearance (lower prevalence of wrinkled appearance, senile dryness, and skin atrophy) independent of factors known to affect skin aging.

Lower intakes of vitamin C were significantly associated with the prevalence of a wrinkled appearance and senile dryness, independent of age, sun exposure, race, menopausal status, energy intake, education, family income, BMI, supplement use, and physical activity. To our knowledge, this is the first study to directly relate dietary intakes of vitamin C with skin aging. In skin, vitamin C exerts different biologic roles, including participation in collagen synthesis, the regeneration process, and wound repair (29). Vitamin C is an important antioxidant found in the skin and may lower the prevalence of wrinkles and senile dryness by its actions as an antioxidant (29). Moreover, several studies have shown that vitamin C has photoprotective properties through oral or topical applications (17). Topical application of vitamin C shows photoprotective properties and suggests improvements of wrinkles (30, 31). Reviewing dietary supplementation, Boelsma et al (16) identified 4 studies that showed a photoprotective effect of vitamin C on skin. Those studies were short-term supplementation trials with high doses of vitamin C and in combination with vitamin E, whereas our findings are from habitual intakes of vitamin C from food sources.

Our results also suggest that a higher dietary intake of linoleic acid has a beneficial role in reducing the chances of developing senile dryness and skin atrophy in middle-aged women. Linoleic acid (n−6 PUFA) is an essential fatty acid that cannot be produced endogenously and is converted after ingestion to other PUFAs such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The association between linoleic acid intake and skin aging has not been investigated; however, several studies have examined the photoprotective effects of EPA and DHA intakes from fish-oil supplements (16, 17). Topical application of EPA has also showed photoprotective properties (32). Linoleic acid may therefore lower the prevalence of senile dryness and skin atrophy by acting as a source of EPA and DHA. Furthermore, low intake of linoleic acid can lead to dermatitis with marked abnormalities (16, 33), and this could also be important in its role in skin-aging appearance.

Our results also suggest that a higher dietary intake of fats and carbohydrates has a negative role in skin-aging appearance. To our knowledge this is the first study to show an association between dietary intakes of fats and carbohydrates with features of skin aging. Furthermore, higher thiamine intakes were associated with an increased likelihood of a wrinkled appearance. Thiamine is an essential B vitamin found in enriched cereals and whole grains. More research is needed to understand these associations.

Our findings add evidence to a predominantly supplement and topical application-based hypothesis that what we eat affects our skin-aging appearance. One other study by Purba et al (18) has reported a significant effect of vegetables, fruit, and olive oil on wrinkles; however, they examined the effect on skin surface microstructure photodamage, whereas in our study we looked at the effect of nutrient intakes on visual features of skin aging that

were determined by trained dermatologists. Because most existing evidence comes from supplemental trials or topical application of nutrients (16–18, 30–32, 34), our study adds to the existing evidence in this field, because it examined nutrient intakes from foods rather than from nutritional supplements.

Although vitamin A has long been noted to have antiwrinkle properties, and retinol (vitamin A) is commonly used in the cosmetics industry as a topical antiwrinkle agent (34, 35), clinical trials have failed to show this effect when taken orally as supplements. Our findings that women with a wrinkled appearance had lower vitamin A intakes support the evidence that vitamin A benefits skin-aging appearance. We also found that women with a wrinkled appearance had lower protein intakes. Lower protein intakes in older adults were shown to increase skin fragility (36). Vitamin A and protein however did not affect the prevalence of a wrinkled appearance in the multivariate-adjusted logistic regression models.

The favorable association of vitamin C and linoleic acid intakes with skin aging may be attributed to the dietary sources of these nutrients. At the time of this survey, the main sources of vitamin C in the US diet were orange juice (more than a quarter of total vitamin C intake), citrus fruit, fruit juices, and tomatoes (37). Linoleic acid is found in oils such as rapeseed and soybean oils and in foods such as green leafy vegetables and nuts (38). Furthermore, as mentioned earlier, the body can convert linoleic acid into EPA and DHA (n−3 PUFAs). These nutrients were not measured in NHANES I, but their main dietary sources are fish and fish oils (39). Current dietary recommendations promote higher intakes of fruit and vegetables and fish and PUFAs (13, 40, 41). Despite several campaigns to promote the consumption of fruit and vegetables and the evidence that diets poor in fruit and vegetables are associated with poor health outcomes, most adults are still not eating enough fruit and vegetables (42, 43). Therefore, a benefit for skin-aging appearance from eating aspects of a healthy diet, such as fruit, vegetables, nuts, and fish, and reducing fat intake may motivate people and improve current promotions for healthy eating.

Our findings need to be interpreted while considering some limitations. This study is a cross-sectional analysis, and no conclusions about the direction of associations between nutrient intakes and skin-aging appearance can be determined. NHANES I data were collected in 1971–1975 and a cohort effect cannot be ruled out. Furthermore, changes in nutrient intakes have occurred in the past 30 y (44); hence, extrapolation to current populations might be affected. Although we used NHANES I data, which has a well-characterized population with good measures of a number of variables such as age, sun exposure, race, BMI, and menopausal status, allowing potential confounding to be controlled for, residual confounding cannot be discarded. One factor that was not measured was the use of facial cosmetics. Nevertheless, on the basis of current knowledge we cannot determine whether use of such products is modified by nutrient intake. The dermatologic component of this survey was not designed to specifically detect associations between nutrients and skin appearance; therefore, post hoc analyses have to be interpreted with caution. However, few studies exist in which comprehensive measures of both dietary intake data and skin-aging appearance are present and thus can be used to test the hypothesis of this study. The dietary data were collected using a 24-h dietary recall. Estimates from a single day of intake may not represent usual, long-term intakes, because of day-to-day variation in the subjects' food intakes.

However, this study used trained interviewers to improve data collection.

This is the first study to examine the effect of nutrient intakes rather than supplements on skin-aging appearance. Our findings suggest that higher intakes of vitamin C and linoleic acid are associated with a lower prevalence of a wrinkled appearance, senile dryness, and skin atrophy, whereas higher intakes of fats and carbohydrates are associated with a higher likelihood of features of skin aging. The favorable associations may be attributable to the dietary sources of these nutrients (fruit, vegetables, and nuts) and are independent of factors known to affect skin aging. Perhaps appealing benefits such as reducing skin-aging appearance may motivate healthy eating, and new campaigns to promote healthy dietary behaviors could consider this issue. Our findings support current recommendations that promote aspects of a healthy diet such as higher intakes of fruit, vegetables, and nuts and indicate a new direction for nutrition research in relation to public health.

REFERENCES

1. Gilchrest BA. Skin aging and photoaging: an overview. J Am Acad Dermatol 1989;21:610–3.
2. Gomez EC, Berman B. The aging skin Clin Geriatr Med 1985;1:285–305.
3. Warren R, Gartstein V, Kligman AM, Montagna W, Allendorf RA, Ridder GM. Age, sunlight, and facial skin: a histologic and quantitative study. J Am Acad Dermatol 1991;25:751–60.
4. Guinot C, Malvy DJ, Ambroisine L, et al. Relative contribution of intrinsic vs extrinsic factors to skin aging as determined by a validated skin age score. Arch Dermatol 2002;138:1454–60.
5. Rexbye H, Petersen I, Johansens M, Klitkou L, Jeune B, Christensen K. Influence of environmental factors on facial ageing. Age Aging 2006; 35:110–5.
6. Kennedy C, Bastiaens MT, Bajdik CD, Willemze R, Westendorp RG, Bouwes Bavinck JN. Effect of smoking and sun on the aging skin. J Invest Dermatol 2003;120:548–54.
7. Leung WC, Harvey I. Is skin ageing in the elderly caused by sun exposure or smoking. Br J Dermatol 2002;147:1187–91.
8. Yin L, Morita A, Tsuji T. Skin aging induced by ultraviolet exposure and tobacco smoking: evidence from epidemiological and molecular studies. Photodermatol Photoimmunol Photomed 2001;17:178–83.
9. Kadunce DP, Burr R, Gress R, Kanner R, Lyon JL, Zone JJ. Cigarette smoking: risk factor for premature facial wrinkling. Ann Intern Med 1991;114:840–4.
10. Dalgard F, Svensson A, Holm JO, Sundby J. Self-reported skin morbidity among adults: associations with quality of life and general health in a Norwegian survey. J Investig Dermatol Symp Proc 2004;9:120–5.
11. Purba MB, Kouris-Blazos A, Wattanapenpaiboon N, et al. Can skin wrinkling in a site that has received limited sun exposure be used as a marker of health status and biological age. Age Aging 2001;30:227–34.
12. Christensen K, Iachina M, Rexbye H, et al. "Looking old for your age": genetics and mortality. Epidemiology 2004;15:251–2.
13. Diet, nutrition and the prevention of chronic diseases. World Health Organ Tech Rep Ser 2003;916:i–viii, 1–149, backcover.
14. Sheretz E, Goldsmith LA. Nutritional influences on the skin. In: Goldsmith LA, ed. Physiology, biochemistry, and molecular biology of the skin. New York, NY Oxford University Press, 1991:1315–28.
15. Miller SJ. Nutritional deficiency and the skin. J Am Acad Dermatol 1989;21:1–30.
16. Boelsma E, Hendriks HF, Roza L. Nutritional skin care: health effects of micronutrients and fatty acids. Am J Clin Nutr 2001;73:853–64.
17. Sies H, Stahl W. Nutritional protection against skin damage from sunlight. Annu Rev Nutr 2004;24:173–200:173–200.
18. Purba MB, Kouris-Blazos A, Wattanapenpaiboon N, et al. Skin wrinkling: can food make a difference. J Am Coll Nutr 2001;20:71–80.
19. US Department of Health and Human Services (1971-1975). National Center for Health Statistics. First National Health and Nutrition Examination Survey (NHANES I), 1971-1975, Hyattsville, MD: Centers for Disease Control and Prevention, 1975.
20. Miller HW. Plan and operation of the Health and Nutrition Examination Survey. United States–1971–1973. Vital Health Stat 1 1973; (10a):1–46.
21. Plan and operation of the Health and Nutrition Examination Survey: United States 1971–1973. Vital Health Stat 1 1973;(10b):1–77.
22. Dunn LB, Damesyn M, Moore AA, Reuben DB, Greendale GA. Does estrogen prevent skin aging? Results from the First National Health and Nutrition Examination Survey (NHANES I). Arch Dermatol 1997;133: 339–42.
23. Part 15a: instruction manual, data collection–examination staff procedures manual for the Health and Nutrition Examination Survey, United States 1971-1973. Washington DC: National Center for Health Statistics, 1972.
24. Johnson ML. Defining the burden of skin disease in the United States–a historical perspective. J Investig Dermatol Symp Proc 2004; 9:108–10.
25. Watt BK, Merrill AL. Agriculture handbook no. 8: composition of foods: raw, processed, prepared. Consumer and Food Economics Research Division United States Department of Agriculture (USDA). Washington DC: US Government Printing Office, 1963.
26. Abraham S, Johnson CL, Najjar MF. Weight and height of adults 18–74 years of age. United States, 1971–74. Vital Health Stat 11 1979;(211): 1–49.
27. Hosmer DW, Lemeshow S. Applied logistic regression. New York, NY: Wiley, 2000.
28. McCarthy SN, Robson PJ, Livingstone MB, et al. Associations between daily food intake and excess adiposity in Irish adults: towards the development of food-based dietary guidelines for reducing the prevalence of overweight and obesity. Int J Obes (Lond) 2006;30: 993–1002.
29. Catani MV, Savini I, Rossi A, Melino G, Avigliano L. Biological role of vitamin C in keratinocytes. Nutr Rev 2005;63:81–90.
30. Raschke T, Koop U, Dusing HJ, et al. Topical activity of ascorbic acid: from in vitro optimization to in vivo efficacy. Skin Pharmacol Physiol 2004;17:200–6.
31. Humbert PG, Haftek M, Creidi P, et al. Topical ascorbic acid on photoaged skin. Clinical, topographical and ultrastructural evaluation: double-blind study vs. placebo Exp Dermatol 2003;12:237–44.
32. Kim HH, Cho S, Lee S, et al. Photoprotective and anti-skin-aging effects of eicosapentaenoic acid in human skin in vivo. J Lipid Res 2006;47: 921–30.
33. Horrobin DF. Essential fatty acid metabolism and its modification in atopic eczema. Am J Clin Nutr 2000;71(suppl):367S–72S.
34. Lee MS, Lee KH, Sin HS, Um SJ, Kim JW, Koh BK. A newly synthesized photostable retinol derivative (retinyl N-formyl aspartamate) for photodamaged skin: profilometric evaluation of 24-week study. J Am Acad Dermatol 2006;55:220–4.
35. Chiu A, Kimball AB. Topical vitamins, minerals and botanical ingredients as modulators of environmental and chronological skin damage. Br J Dermatol 2003;149:681–91.
36. Chernoff R. Protein and older adults. J Am Coll Nutr 2004;23(suppl): 627S–30S.
37. Block G, Dresser CM, Hartman AM, Carroll MD. Nutrient sources in the American diet: quantitative data from the NHANES II survey. I. Vitamins and minerals Am J Epidemiol 1985;122:13–26.
38. Williams CM, Burdge G. Long-chain n−3 PUFA: plant v. marine sources. Proc Nutr Soc 2006;65:42–50.
39. Meyer BJ, Mann NJ, Lewis JL, Milligan GC, Sinclair AJ, Howe PR.

Dietary intakes and food sources of omega-6 and omega-3 polyunsaturated fatty acids. Lipids 2003;38:391–8.

40. US Department of Health and Human Services and US Department of Agriculture. Dietary guidelines for Americans, 2005. 6th ed. Washington, DC: US Government Printing Office, 2005.

41. New guidelines focus on fish oil, omega-3 fatty acids. FDA Consum 2003;37:7.

42. Guenther PM, Dodd KW, Reedy J, Krebs-Smith SM. Most Americans eat much less than recommended amounts of fruits and vegetables. J Am Diet Assoc 2006;106:1371–9.

43. Thompson B, Mark-Wahnefried W, Taylor G, et al. Baseline fruit and vegetable intake among adults in seven 5 a day study centers located in diverse geographic areas. J Am Diet Assoc 1999;99:1241–8.

44. Kant AK, Graubard BI. Secular trends in patterns of self-reported food consumption of adult Americans: NHANES 1971–1975 to NHANES 1999–2002. Am J Clin Nutr 2006;84:1215–23.

acid during methotrexate therapy of rheumatoid arthritis: results from a double-blind, placebo-controlled trial. Ann Intern Med 1994;121:833–41.

3. Alarcón G, Tracy I, Blackburn W. Methotrexate in rheumatoid arthritis: toxic effects as the major factor in limiting long-term treatment. Arthritis Rheum 1989;32:671–6.
4. Baggott JE, Morgan SL, Ha TS, Vaughn WH, Hine RJ. Inhibition of folate-dependent enzymes by non-steroidal anti-inflammatory drugs. Biochem J 1992;282:197–202.
5. Sathi N, Dawson J. Methotrexate-induced pancytopenia associated with co-prescription of penicillin and trimethoprim. Clin Rheumatol 2007; 26:134–5.
6. Pincus T, Yazici Y, Sokka T, Aletaha D, Smolen J. Methotrexate as the "Anchor Drug" for the treatment of early rheumatoid arthritis. Clin Exp Rheumatol 2003;21(suppl):S179–85.
7. Smolen J, Aletha D, Machold K. Therapeutic strategies in early rheumatoid arthritis. Best Pract Res Clin Rheumatol 2005;19:163–77.
8. Arabelovic S, Sam G, Dalla GE, et al. Preliminary evidence shows that folic acid fortification of the food supply is associated with higher methotrexate dosing in patient with rheumatoid arthritis. J Am Coll Nutr 2007;26:453–5.
9. Khanna D, Park GS, Paulus HE, et al. Reduction of the efficacy of methotrexate by the use of folic acid: post hoc analysis from two randomized controlled studies. Arthritis Rheum 2005;52:3030–8.
10. Morgan SL, Baggott JE, Alarcón GS. Effect of folic acid supplementation on the efficacy of methotrexate treatment in rheumatoid arthritis: comment on the article by Khanna et al. Arthritis Rheum 2006;54: 1708–9.

Reply to E Baggott and SL Morgan

Dear Sir:

We agree with Baggott and Morgan that folic acid or its derivatives are valuable in reducing the toxic side effects of methotrexate in patients with rheumatoid arthritis (RA) and, indeed, we (1) pointed this out (page 523). However, we do not think we made a conceptual error in our "thought experiment": what we wrote was that studies need to be done to determine whether the incidence or severity of RA and psoriasis have changed in countries that have introduced folic acid fortification. We also asked whether treatment choice or drug efficacy has changed in these countries. The report by Arabelovic et al (2) that appeared after our Commentary was submitted shows that the average dose of methotrexate used has increased in the United States since 1996; the explanation offered by Baggott and Morgan is just as speculative as the suggestion that this change is a consequence of fortification. A key question is whether Baggott and Morgan consider it ethical to give additional folic acid to untreated RA patients to see whether it changes their symptoms, even if such a trial were to take place in a country without fortification. We think not. Finally, to say that there is no evidence that fortification has increased the incidence of RA simply reflects the fact that no such study has been conducted. We believe that such studies should be conducted, in the same way as they have been to determine the incidence of cancer (3). What we need is more evidence.

No conflicts of interest were declared.

A David Smith
Helga Refsum

OPTIMA
Department of Physiology
Anatomy & Genetics
University of Oxford
Oxford
United Kingdom
david.smith@pharm.ox.ac.uk

REFERENCES

1. Smith AD, Kim YI, Refsum H. Is folic acid good for everyone? Am J Clin Nutr 2008;87:517–33.
2. Arabelovic S, Sam G, Dallal GE, et al. Preliminary evidence shows that folic acid fortification of the food supply is associated with higher methotrexate dosing in patients with rheumatoid arthritis. J Am Coll Nutr 2007;26:453–5.
3. Mason JB, Dickstein A, Jacques PF, et al. A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis. Cancer Epidemiol Biomarkers Prev 2007;16:1325–9.

Erratum

Cosgrove MC, Franco OH, Granger SP, Murray PG, Mayes AE. Dietary nutrient intakes and skin-aging appearance among middle-aged American women. Am J Clin Nutr 2007;86:1225–31.

In the third paragraph in the left-hand column on page 1229, the following sentence should have been deleted: "Linoleic acid … is converted after ingestion to other PUFAs such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)." In the same paragraph, the following sentence also should have been deleted: "Linoleic acid may therefore lower the prevalence of senile dryness and skin atrophy by acting as a source of EPA and DHA." Finally, in the second full paragraph of the right-hand column on page 1229, the following sentence should have been deleted as well: "Furthermore, as mentioned earlier, the body can convert linoleic acid into EPA and DHA (n–3 PUFAs)."