Intake of Purine-Rich Foods, Protein, and Dairy Products and Relationship to Serum Levels of Uric Acid

The Third National Health and Nutrition Examination Survey

Hyon K. Choi,[1] Simin Liu,[2] and Gary Curhan[2]

Objective. Various commonly consumed foods have long been suspected of affecting the serum uric acid level, but few data are available to support or refute this impression. Our objective was to evaluate the relationship between dietary factors and serum uric acid levels in a nationally representative sample of men and women in the US.

Methods. Using data from 14,809 participants (6,932 men and 7,877 women) ages 20 years and older in the Third National Health and Nutrition Examination Survey (for the years 1988–1994), we examined the relationship between the intake of purine-rich foods, protein, and dairy products and serum levels of uric acid. Diet was assessed with a food-frequency questionnaire. We used multivariate linear regression to adjust for age, sex, total energy intake, body mass index, use of diuretics, β-blockers, allopurinol, and uricosuric agents, self-reported hypertension and gout, serum creatinine level, and intake of alcohol.

Results. The serum uric acid level increased with increasing total meat or seafood intake and decreased with increasing dairy intake. After adjusting for age, the differences in uric acid levels between the extreme quintiles of intake were 0.48 mg/dl for total meat (95% confidence interval [95% CI] 0.34, 0.61; *P* < 0.001 for trend), 0.16 mg/dl for seafood (95% CI 0.06, 0.27; *P* = 0.005 for trend), and –0.21 mg/dl for total dairy intake (95% CI –0.37, –0.04; *P* = 0.02 for trend). After adjusting for other covariates, the differences between the extreme quintiles were attenuated but remained significant (*P* < 0.05 for all comparisons). The total protein intake was not associated with the serum uric acid level in multivariate analyses (*P* = 0.74 for trend). Those who consumed milk 1 or more times per day had a lower serum uric acid level than did those who did not drink milk (multivariate difference –0.25 [95% CI –0.40, –0.09]; *P* < 0.001 for trend). Similarly, those who consumed yogurt at least once every other day had a lower serum uric acid level than did those who did not consume yogurt (multivariate difference –0.26 [95% CI –0.41, –0.12]; *P* < 0.001 for trend).

Conclusion. These findings from a nationally representative sample of adults in the US suggest that higher levels of meat and seafood consumption are associated with higher serum levels of uric acid but that total protein intake is not. Dairy consumption was inversely associated with the serum uric acid level.

[1]Hyon K. Choi, MD, DrPH: Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; [2]Simin Liu, MD, ScD, Gary Curhan, MD, ScD: Brigham and Women's Hospital, Harvard Medical School, and Harvard School of Public Health, Boston, Massachusetts.

Address correspondence and reprint requests to Hyon K. Choi, MD, DrPH, Rheumatology Unit, Bulfinch 165, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114. E-mail: hchoi@partners.org.

Hyperuricemia is considered the precursor of gout, which is the most common form of inflammatory arthritis in adult men (1). Various commonly consumed foods have long been suspected of affecting the serum uric acid levels, but few data are available. For example, patients with hyperuricemia or gout are typically advised to avoid habitual intake of purine-rich foods such as meat and seafood (2,3), but data about the actual relationship between these foods and serum levels of uric acid are scarce. Previous metabolic studies used artificial loading of purified purine (4–7) but did not elucidate the relationship to actual foods. In particular, the relationship between total protein intake and serum uric acid levels remains unclear. Although high-protein diets tend to contain large quantities of purines, the

Table 1. Characteristics of the study subjects, according to quintiles of intake of purine-rich food groups, dairy foods, and protein*

Variable	Daily intake, servings/day	Age, years	Men, %	Alcohol servings/day	BMI, kg/m^2	Diuretic use, %	Uric acid drug use, %†	Creatinine, mg/dl	History of hypertension, %
Total meat									
Quintile 1	0.4	48	39	0.2	26	3	1	1.1	26
Quintile 3	1.0	45	45	0.3	27	2	1	1.1	23
Quintile 5	2.1	41	61	0.4	27	1	1	1.1	21
Seafood									
Quintile 1	0.0	45	44	0.2	27	2	1	1.1	23
Quintile 3	0.1	46	47	0.3	27	3	1	1.1	28
Quintile 5	0.5	45	48	0.3	27	2	1	1.1	24
Dairy foods									
Quintile 1	0.3	46	45	0.3	27	2	1	1.1	26
Quintile 3	1.2	46	47	0.3	27	2	1	1.1	25
Quintile 5	3.0	44	49	0.3	26	2	1	1.1	21
Total protein‡									
Quintile 1	52	40	46	0.4	26	1	1	1.0	26
Quintile 3	81	47	48	0.3	27	3	1	1.1	25
Quintile 5	120	44	47	0.3	27	2	1	1.1	25
All participants	–	45	48	0.3	27	2	1	1.1	24

* Except where indicated otherwise, values are the mean. BMI = body mass index.
† Allopurinol and uricosuric agents.
‡ Energy-adjusted. Values are in grams per day.

uricosuric effect associated with such diets may, in fact, even lower serum uric acid levels (3,8,9). Furthermore, limited data suggest that there might be an inverse relationship between dairy product consumption and serum uric acid levels (10,11). In a recent large prospective study of incident gout among men, we found that higher meat and seafood intake independently increased the risk of incident gout, while higher dairy intake was protective against the risk (12). Further, higher protein intake did not increase the risk (12). The relationship between these dietary factors and the level of serum uric acid, however, was not examined in this cohort.

In this study based on the Third National Health and Nutrition Examination Survey (NHANES-III), we evaluated the relationship between the intake of purine-rich foods, protein, and dairy products and levels of serum uric acid.

SUBJECTS AND METHODS

Study population. Started in 1988 and completed in 1994, the NHANES-III included a representative sample of the noninstitutionalized civilian population, which was selected by using a multistage, stratified sampling design. Persons 60 years of age and older and African American and Mexican American persons were oversampled. After a home interview, participants were invited to attend examination sessions where blood and urine specimens were obtained. For some participants who were unable to attend the examination because of health reasons, a blood sample was obtained during the home interview.

We limited our primary analyses to participants 20 years of age and older who attended the medical examination.

The 14,809 participants (6,932 men and 7,877 women) with complete information were included in our analyses. In addition, after excluding participants who self-reported gout or were taking allopurinol or uricosuric agents (i.e., probenecid and sulfinpyrazone) (n = 446), we repeated our analyses among the remaining 14,363 participants.

Uric acid measurement. Serum uric acid was measured by oxidization with the specific enzyme uricase to form allantoin and H_2O_2 (Hitachi Model 737 Multichannel Analyzer; Boehringer Mannheim Diagnostics, Indianapolis, IN), as detailed elsewhere (13). Values are reported in milligrams per deciliter (to convert to micromoles per liter, multiply by 59.48).

Dietary assessment. Dietary assessment was based on data from a food frequency questionnaire. Food frequency information was collected during the household interview and has been shown to be a valid and reliable method for assessing average consumption (14,15). Respondents were asked how often over the previous month they had eaten specific food items. From these data, we calculated the average daily intake of each food item. The average daily intakes of each item were then combined to compute the following composite food groups: total meat (beef, including hamburger, steaks, roast beef, and meatloaf; pork and ham, including roast pork, pork chops, and spare ribs; liver and other organ meats, including heart, kidney, tongue, and tripe; bacon, sausage, and luncheon meats, such as hot dogs, salami, and bologna; poultry of all types, including baked or fried chicken nuggets, chicken salad, and turkey); seafood (fish, including fillets, fish sticks, fish sandwiches, and tuna; shrimp, clams, oysters, crab, and lobster); and dairy foods (milk; yogurt and frozen yogurt; ice cream, ice milk, and milkshakes; cheese of all types, including American, Swiss, cheddar, and cottage cheese). The energy fraction from protein, fat, and carbohydrates and the total energy intake were calculated from a 24-hour dietary recall list.

Assessment of covariates. The NHANES-III collected information on body measurements (including height and

Table 2. Serum uric acid level, according to quintiles of intake of purine-rich food groups, dairy foods, and protein*

Variable	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend	Difference per unit increase†
Total meats, servings/day	<0.59	0.59–0.81	0.82–1.11	1.12–1.53	>1.53		
Mean ± SEM	5.17 ± 0.04	5.23 ± 0.05	5.29 ± 0.03	5.40 ± 0.05	5.56 ± 0.06		
Age-adjusted difference	0	0.07	0.16	0.30	0.48	<0.001	0.23
(95% CI)	(Referent)	(−0.05, 0.20)	(0.05, 0.26)	(0.19, 0.41)	(0.34, 0.61)		(0.15, 0.32)
Multivariate difference‡	0	−0.03	0.03	0.04	0.11	0.02	0.06
(95% CI)	(Referent)	(−0.13, 0.06)	(−0.05, 0.12)	(−0.06, 0.14)	(0.01, 0.22)		(0.01, 0.11)
Seafood, servings/day	<0.03	0.04–0.10	0.11–0.16	0.17–0.30	>0.30		
Mean ± SEM	5.23 ± 0.04	5.32 ± 0.04	5.32 ± 0.04	5.36 ± 0.04	5.39 ± 0.04		
Age-adjusted difference	0	0.11	0.08	0.14	0.16	0.005	0.25
(95% CI)	(Referent)	(−0.02, 0.23)	(−0.02, 0.19)	(0.01, 0.27)	(0.06, 0.27)		(0.13, 0.36)
Multivariate difference‡	0	0.06	0.03	0.04	0.10	0.06	0.12
(95% CI)	(Referent)	(−0.05, 0.17)	(−0.05, 0.11)	(−0.06, 0.14)	(0.02, 0.18)		(0.03, 0.22)
Total dairy foods, servings/day	<0.5	0.5–0.9	1.0–1.3	1.4–1.9	>2.0		
Mean ± SEM	5.43 ± 0.05	5.30 ± 0.04	5.35 ± 0.04	5.38 ± 0.05	5.20 ± 0.05		
Age-adjusted difference	0	−0.12	−0.07	−0.03	−0.21	0.02	−0.06
(95% CI)	(Referent)	(−0.27, 0.02)	(−0.20, 0.06)	(−0.18, 0.12)	(−0.37, − 0.04)		(−0.11, −0.02)
Multivariate difference‡	0	−0.14	−0.04	−0.04	−0.19	0.005	−0.05
(95% CI)	(Referent)	(−0.26, −0.03)	(−0.15, 0.08)	(−0.15, 0.07)	(−0.30, −0.09)		(−0.08, −0.02)
Total protein, % of energy	<12	12.1–14	14.1–16	16.1–19	>19		
Mean ± SEM	5.26 ± 0.04	5.24 ± 0.04	5.30 ± 0.05	5.35 ± 0.04	5.48 ± 0.05		
Age-adjusted difference	0	−0.07	0.00	0.08	0.25	0.006	0.03
(95% CI)	(Referent)	(−0.17, 0.04)	(−0.13, 0.13)	(−0.02, 0.17)	(0.12, 0.38)		(0.03, 0.03)
Multivariate difference§	0	−0.07	−0.04	−0.03	0.04	0.23	0.00
(95% CI)	(Referent)	(−0.15, 0.02)	(−0.13, 0.06)	(−0.11, 0.05)	(−0.05, 0.13)		(−0.00, 0.01)

* Values are in mg/dl. 95% CI = 95% confidence interval.
† Differences per additional daily serving are presented for total meats and dairy foods. Difference per additional weekly serving is presented for seafood in order to reflect its distribution. Difference per additional daily 5% of energy is presented for total protein.
‡ Adjusted for age, sex, total energy intake, body mass index, use of diuretics, β-blockers, allopurinol, and uricosuric agents, self-report of hypertension and gout, serum creatinine level, and intake of alcohol, total meats, seafood, and dairy foods.
§ Adjusted for age, sex, total energy intake, body mass index, use of diuretics, β-blockers, allopurinol, and uricosuric agents, self-report of hypertension and gout, serum creatinine level, and intake of alcohol and total fat (% of energy).

weight), alcohol consumption, medication use (including diuretics, antihypertensives, allopurinol, and uricosuric agents), medical conditions (including self-reported hypertension and gout), and serum creatinine levels. The body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters.

Statistical analysis. All statistical analyses were performed using survey commands of Stata software (e.g., SVYMean and SVYReg) to incorporate sample weights and to adjust for clusters and strata of the complex sample design (version 7; Stata, College Station, TX).

We used linear regression to evaluate relationships between food groups and serum uric acid levels. The average daily intake for a food group or an individual food item was categorized into quintiles of intake whenever possible, and each quintile group of intake was compared with the lowest quintile group of intake. When a small stratum size of individual food intake did not allow quintile analysis, we instead used the following categories, representing mean servings per day: 0, 0.01–0.09, 0.1–0.49, 0.5–0.99, and ≥1.0. We repeated our analysis treating food intake (daily servings) as a continuous variable.

Multivariate models were adjusted for age, sex, total energy intake, BMI, use of diuretics, β-blockers, allopurinol, and uricosuric agents, self-reported hypertension and gout, serum creatinine level, and intake of alcohol, total meats, seafood, and dairy foods. In the multivariate nutrient-density model for protein intake (16), we simultaneously included energy intake, the percentages of energy derived from protein and fat, and other covariates. The coefficients from this model can be interpreted as the estimated effect of substituting a specific percentage of energy from protein for the same percentage of energy from carbohydrates (16). We repeated these analyses using energy-adjusted protein values (16) instead of nutrient density.

Trends in serum uric acid levels across quintiles of intake were assessed in linear regression models by using the median values of each quintile to minimize the influence of outliers. We also performed logistic regressions with a dichotomous variable of hyperuricemia (i.e., serum uric acid >7.0 mg/dl for men and >5.7 mg/dl for women [13]) adjusting for the same covariates.

We explored potential interactions by sex, BMI (<25 kg/m² versus ≥25 kg/m²), and alcohol use (abstainer versus drinker) by testing the significance of interaction terms added to our final multivariate models. For all difference estimates, we calculated 95% confidence intervals (95% CIs). All P values are 2-sided.

RESULTS

The mean age of the study population was 45 years. The mean serum uric acid level was 5.32 mg/dl

Table 3. Serum uric acid level, according to quintiles or categories of intake of individual foods*

Variable†	Level of consumption of individual foods					P for trend
	Quintile or category 1	Quintile or category 2	Quintile or category 3	Quintile or category 4	Quintile or category 5	
Beef, servings/day	<0.13	0.13–0.23	0.26–0.33	0.34–0.56	≥0.57	
Age-adjusted difference	0	0.29	0.09	0.28	0.45	<0.001
(95% CI)	(Referent)	(0.10, 0.49)	(−0.01, 0.20)	(0.18, 0.38)	(0.33, 0.56)	
Multivariate difference	0	0.10	0.02	0.13	0.24	<0.001
(95% CI)	(Referent)	(−0.06, 0.25)	(−0.07, 0.11)	(0.04, 0.22)	(0.13, 0.35)	
Pork and ham, servings/day	<0.02	0.03–0.06	0.07–0.13	0.14–0.17	≥0.18	
Age-adjusted difference	0	0.03	0.08	0.10	0.27	<0.001
(95% CI)	(Referent)	(−0.09, 0.15)	(−0.01, 0.18)	(−0.16, 0.36)	(0.18, 0.35)	
Multivariate difference	0	−0.06	0.01	−0.03	0.11	0.003
(95% CI)	(Referent)	(−0.17, 0.04)	(−0.06, 0.09)	(−0.22, 0.16)	(0.04, 0.19)	
Processed meats, servings/day	<0.04	0.05–0.09	0.13–0.16	0.17–0.43	>0.44	
Age-adjusted difference	0	0.05	0.15	0.32	0.48	<0.001
(95% CI)	(Referent)	(−0.08, 0.18)	(0.03, 0.28)	(0.19, 0.45)	(0.34, 0.61)	
Multivariate difference	0	−0.03	0.02	0.10	0.22	<0.001
(95% CI)	(Referent)	(−0.14, 0.09)	(−0.08, 0.12)	(0.00, 0.21)	(0.11, 0.34)	
Poultry, servings/day	<0.13	0.14–0.20	0.21–0.30	0.31–0.43	>0.44	
Age-adjusted difference	0	0.21	−0.01	0.01	0.00	0.83
(95% CI)	(Referent)	(0.05, 0.37)	(−0.10, 0.08)	(−0.12, 0.13)	(−0.11, 0.11)	
Multivariate difference	0	0.15	−0.01	−0.04	−0.02	0.46
(95% CI)	(Referent)	(0.01, 0.28)	(−0.09, 0.08)	(−0.13, 0.06)	(−0.12, 0.07)	
Liver and organ meats, servings/day	0	0.01–0.09	>0.1	–	–	
Age-adjusted difference	0	0.07	0.02			0.40
(95% CI)	(Referent)	(−0.01, 0.15)	(−0.12, 0.15)			
Multivariate difference	0	−0.01	0.00			0.86
(95% CI)	(Referent)	(−0.08, 0.06)	(−0.13, 0.12)			
Fish, servings/day	0	0.01–0.09	0.1–0.49	>0.5	–	
Age-adjusted difference	0	0.13	0.10	0.30		0.023
(95% CI)	(Referent)	(0.04, 0.22)	(0.02, 0.18)	(0.08, 0.52)		
Multivariate difference	0	0.10	0.04	0.26		0.007
(95% CI)	(Referent)	(0.02, 0.18)	(−0.03, 0.11)	(0.11, 0.41)		
Other seafood, servings/day	0	0.01–0.09	>0.1	–	–	
Age-adjusted difference	0	0.10	0.24			<0.001
(95% CI)	(Referent)	(0.01, 0.18)	(0.12, 0.36)			
Multivariate difference	0	0.03	0.17			0.004
(95% CI)	(Referent)	(−0.04, 0.11)	(0.06, 0.29)			
Milk, servings/day	0	0.01–0.09	0.1–0.49	0.5–0.99	≥1.0	
Age-adjusted difference	0	0.04	0.03	−0.02	−0.18	0.014
(95% CI)	(Referent)	(−0.14, 0.21)	(−0.12, 0.18)	(−0.15, 0.11)	(−0.39, 0.04)	
Multivariate difference	0	−0.05	−0.05	−0.07	−0.25	<0.001
(95% CI)	(Referent)	(−0.19, 0.09)	(−0.17, 0.07)	(−0.17, 0.04)	(−0.40, −0.09)	
Yogurt, servings/day	0	0.01–0.09	0.1–0.49	≥0.5	–	
Age-adjusted difference	0	−0.24	−0.40	−0.52		<0.001
(95% CI)	(Referent)	(−0.38, −0.09)	(−0.52, −0.28)	(−0.69, −0.34)		
Multivariate difference	0	−0.10	−0.23	−0.26		<0.001
(95% CI)	(Referent)	(−0.21, 0.02)	(−0.34, −0.11)	(−0.41, −0.12)		
Cheese, servings/day	0	0.01–0.09	0.1–0.49	0.5–0.99	≥1.0	
Age-adjusted difference	0	−0.07	−0.09	0.03	−0.08	0.16
(95% CI)	(Referent)	(−0.22, 0.09)	(−0.23, 0.06)	(−0.11, 0.17)	(−0.44, 0.29)	
Multivariate difference	0	−0.09	−0.15	−0.09	−0.30	0.50
(95% CI)	(Referent)	(−0.20, 0.03)	(−0.25, −0.04)	(−0.21, 0.03)	(−0.68, 0.08)	

* The average daily intake for individual foods was categorized into quintiles of intake whenever possible (i.e., beef, pork and ham, processed meats, and poultry). When the small stratum size of individual food intake did not allow quintile analysis (i.e., liver and organ meats, fish, other seafood, milk, yogurt, and cheese), we used the following categories of mean servings per day: 0, 0.01–0.09, 0.1–0.49, 0.5–0.99, and ≥1.0. Processed meats represents bacon, sausage (chorizo), hot dogs, salami, and bologna. Other seafood represents shrimp, clam, crab, lobster, and oyster. Serum uric acid values are in mg/dl. 95% CI = 95% confidence interval.

† Multivariate linear regression models were adjusted for age, sex, total energy intake, body mass index, use of diuretics, β-blockers, allopurinol, and uricosuric agents, self-report of hypertension and gout, serum creatinine level, and alcohol intake. In addition, multivariate differences for *individual meat items* were adjusted for seafood and dairy foods, multivariate differences for *individual seafood items* were adjusted for total meats and dairy foods, and multivariate differences for *individual dairy items* were adjusted for total meats and seafood.

(6.07 mg/dl among men and 4.65 mg/dl among women), and 18% had hyperuricemia (19% among men and 17% among women). The mean serum uric acid levels were similar across race/ethnicity categories (i.e., white, African American, Mexican American, and other). The characteristics according to intake of purine-rich food groups, dairy foods, and total protein are shown in Table 1. With increasing intake of meat, the age tended to decrease, the proportion of males increased, and daily alcohol intake slightly increased. Hypertension tended to be less common with increasing intake of meat and dairy foods.

The serum uric acid level increased with increasing total meat or seafood intake (Table 2). After adjusting for age, the serum uric acid level in the highest quintile group of total meat intake was higher than that in the lowest quintile by 0.48 mg/dl (95% CI 0.34, 0.61; $P < 0.001$ for trend). The corresponding difference for seafood was 0.16 mg/dl and (95% CI 0.06, 0.27; $P = 0.005$ for trend). After adjusting for other covariates, these differences between the extreme quintiles were attenuated but remained significant ($P < 0.05$ for both comparisons) (Table 2).

In the age-adjusted analysis for individual meat items, the differences in serum uric acid levels between the extreme quintiles of intake were 0.45 mg/dl (95% CI 0.33, 0.56) for beef, 0.27 mg/dl (95% CI 0.18, 0.35) for pork, and 0.48 mg/dl (95% CI 0.34, 0.61) for processed meats. These magnitudes were attenuated, but remained significant, after multivariate adjustment (Table 3). Similarly, higher intake of individual seafood items was associated with higher level of serum uric acid (Table 3).

After adjusting for age, the serum uric acid level in the highest quintile group of total dairy food intake was lower than that in the lowest by 0.21 mg/dl (95% CI 0.04, 0.37; $P = 0.02$ for trend). After adjusting for other covariates, the difference between the extreme quintiles remained similar ($P = 0.005$ for trend) (Table 2). Those who consumed milk ≥ 1 time per day had a lower serum uric acid level than did those who did not drink milk (multivariate difference -0.25 [95% CI -0.40, -0.09]; $P < 0.001$ for trend) (Table 3). Similarly, those who consumed yogurt at least once every other day had a lower uric acid level than did those who did not consume yogurt (multivariate difference -0.26 [95% CI -0.41, -0.12]; $P < 0.001$ for trend).

The results of logistic regressions with hyperuricemia as a dichotomous outcome were similar. For example, the multivariate odds ratio (OR) for hyperuricemia among those in the highest quintile group of meat intake as compared with those in the lowest quintile was 1.37 (95% CI 1.05, 1.80; $P = 0.027$ for trend) and the corresponding OR for dairy intake was 0.74 (95% CI 0.55, 0.99; $P = 0.05$ for trend). The multivariate ORs for hyperuricemia were 1.58 (95% CI 1.07, 2.34; $P = 0.11$ for trend) for fish consumption between more than a half daily serving and none, and 0.66 (95% CI 0.48, 0.89; $P = 0.011$ for trend) for milk consumption between >1 daily serving and none.

The serum uric acid level increased with increasing protein intake in the age-adjusted analysis ($P = 0.006$ for trend). However, after adjusting for other covariates, total protein intake was no longer associated with the serum uric acid level (Table 2). When we repeated the analysis using energy-adjusted protein values (16) instead of the percentage of energy, the results did not materially change ($P = 0.72$ for trend).

When we repeated our analyses for foods or protein after excluding participants who self-reported gout or were taking allopurinol or uricosuric agents, the results did not materially change. There were no significant interactions between total meat or seafood intake and sex, BMI, or alcohol use ($P > 0.27$ for interaction for all comparisons). The serum uric acid level in the highest quintile group of dairy food intake was lower than that in the lowest quintile by 0.14 mg/dl (95% CI 0.03, 0.25) among those with a BMI <25 kg/m^2 and by 0.30 mg/dl (95% CI 0.13, 0.47) among those with a BMI ≥ 25 kg/m^2 ($P = 0.13$ for interaction).

DISCUSSION

In this nationally representative sample of men and women, the serum uric acid level was found to significantly increase with increasing consumption of meat and seafood but not with total protein intake. In addition, we found a significant inverse association with dairy consumption. These associations were independent of both the other dietary factors we studied and the other risk factors for hyperuricemia, such as age, sex, BMI, serum creatinine level, hypertension, alcohol use, and diuretic use.

The current study findings suggest that the consumption of meat and seafood in amounts reflective of the nationwide intake increases serum levels of uric acid. Previously, the link has been primarily extrapolated from animal or human metabolic experiments that examined the impact of short-term artificial loading of purified purine (rather than actual food items) on the serum uric acid level (4–7). However, the precise identity and quantity of individual purines in most foods are not well-known, especially when cooked or processed (8),

and the bioavailability of various purines contained in different foods varies substantially. For example, dietary substitution/addition experiments showed that RNA has a greater effect on the serum uric acid level than does an equivalent amount of DNA (7), ribomononucleotides greater than nucleic acid (17), and adenine greater than guanine (4). Thus, it has been difficult to predict whether a commonly consumed food or food group actually affects the serum uric acid level, and if so, then by how much. The current study directly linked common foods and serum uric acid levels and provides the relevant information.

We found a significant inverse relationship between dairy consumption and serum uric acid levels, which is consistent with previous reports (10,11). Ingestion of milk proteins (casein and lactalbumin) has been shown to decrease serum uric acid levels in healthy subjects via the uricosuric effect of these proteins (11). Conversely, in a 4-week randomized clinical trial, it was shown that a significant increase in serum uric acid levels was induced by consumption of a dairy-free diet (11). Since dairy products are low in purine content, dairy protein may exert its urate-lowering effect without having the concomitant purine load contained in other protein sources, such as meat and seafood.

The total protein intake was not associated with the uric acid level. Protein-rich foods have been generally perceived as surrogates for purine-rich foods, and patients with gout and hyperuricemia have been traditionally advised to reduce their protein intake. While we are not aware of any direct evidence that ingested proteins per se cause hyperuricemia, there are reports that suggest the contrary (8,9,18). High-protein diets are associated with increased urinary excretion of uric acid and may lower serum levels of uric acid (8,9,18). A small retrospective case–control study showed that protein consumption was slightly lower in gout patients than controls, although the difference was not statistically significant (8). Overall, our findings are consistent with these previous studies. These data collectively suggest that protein per se does not increase uric acid levels and that the protein content of foods may not be a correct surrogate for purine content.

Strengths and limitations of our study deserve comment. This study was performed in a nationally representative sample of women and men in the US; thus, the findings are likely to be generalizable to men and women in the US. A cross-sectional study design, as opposed to cohort studies, tends to leave uncertainty regarding the temporal sequence of exposure–outcome relationships and is also vulnerable to recall bias. If some participants reduced their intake of meat or seafood based on previously identified hyperuricemia, it would lead to an underestimation of the association between dietary intake and serum uric acid level, making our findings conservative. In the NHANES-III, the health examination component that included serum uric acid measurement (outcome) was performed after the household interview that inquired about dietary intake during the previous month (exposure). Thus, it appears implausible that the serum uric acid levels measured in this study would somehow systematically influence the reported intake of these factors. Our main analysis included those with self-reported gout and those who were taking medications to treat hyperuricemia. Thus, if these participants reduced their intake of meat or seafood based on their diagnosis of gout or hyperuricemia requiring treatment, it would theoretically lead to an underestimation of the association between these foods and the serum uric acid level. However, exclusion of these participants did not materially affect our results. This is likely due to the low proportion of participants with these characteristics (3%) or is potentially due to an insubstantial change in diet after their diagnosis of gout or hyperuricemia requiring treatment.

In conclusion, our results suggest that higher levels of meat and seafood consumption are associated with higher levels of serum uric acid, but the total protein intake is not. Dairy consumption was inversely associated with the uric acid level.

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