High school dietary dairy intake and teenage acne

Clement A. Adebamowo, MD, ScD,[a,g] Donna Spiegelman, ScD,[b,c] F. William Danby, MD,[f] A. Lindsay Frazier, MD,[d,e] Walter C. Willett, MD, DrPH,[a,c,e] and Michelle D. Holmes, MD, DrPH[e]
Boston, Massachusetts; Hanover, New Hampshire; and Ibadan, Nigeria

Background: Previous studies suggest possible associations between Western diet and acne. We examined data from the Nurses Health Study II to retrospectively evaluate whether intakes of dairy foods during high school were associated with physician-diagnosed severe teenage acne.

Methods: We studied 47,355 women who completed questionnaires on high school diet in 1998 and physician-diagnosed severe teenage acne in 1989. We estimated the prevalence ratios and 95% confidence intervals of acne history across categories of intakes.

Results: After accounting for age, age at menarche, body mass index, and energy intake, the multivariate prevalence ratio (95% confidence intervals; *P* value for test of trend) of acne, comparing extreme categories of intake, were: 1.22 (1.03, 1.44; .002) for total milk; 1.12 (1.00, 1.25; .56) for whole milk; 1.16 (1.01, 1.34; .25) for low-fat milk; and 1.44 (1.21, 1.72; .003) for skim milk. Instant breakfast drink, sherbet, cottage cheese, and cream cheese were also positively associated with acne.

Conclusion: We found a positive association with acne for intake of total milk and skim milk. We hypothesize that the association with milk may be because of the presence of hormones and bioactive molecules in milk. (J Am Acad Dermatol 2005;52:207-14.)

Acne is one of the common diseases of the skin and about $4 billion is spent on treatment yearly.[1] There are also significant social and emotional costs.[2] Although acne affects all ages in Western countries, prevalence starts to increase from the age of 4 years, and peaks at 16 to 18 years when 75% to 98% of the population is affected.[3]

Acne results from hyperkeratinization and obstruction of the pilosebaceous follicles secondary to androgen-stimulated failure of normal desquamation of the follicular epithelium, androgen-stimulated sebum production, colonization of the follicles by *Propionibacterium* acne, and, variably, inflammation.[4] Of these factors, androgens (testosterone and 5α-reduced steroids) and their interaction with receptors of varying sensitivities on the pilosebaceous germinative epithelia are probably the most important.

An association between diet and acne has long been postulated but remains unproven.[1,5] Ecologic studies have suggested that the incidence of acne is low in non-Western societies and increases with adoption of Western diet.[5] A wide variety of food items have been postulated to be associated with

From the Departments of Nutrition,[a] Biostatistics,[b] and Epidemiology,[c] Harvard School of Public Health; Division of Pediatric Oncology, Dana-Farber Cancer Institute, Harvard Medical School[d]; Channing Laboratory, Department of Medicine, Brigham and Women's Hospital[e]; Dartmouth Medical School[f]; and the Division of Oncology, Department of Surgery, University of Ibadan, University College Hospital.[g]

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Reprint requests: Clement A. Adebamowo, MD, ScD, Department of Nutrition, Harvard School of Public Health, 665 Huntington Ave, Boston, MA 02115. E-mail: clement.adebamowo@channing.harvard.edu.

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acne including milk and other dairy products,[6] chocolate, cereal, bread, nuts, eggs, and pork.[1] Others have believed that specific nutrients such as carbohydrates, fats, or nonnutrient dietary variables such as high-glycemic index foods, and salt are more important. The results of case series, however, have not consistently supported any dietary factor.[5] Apart from a clinical trial of the effect of chocolate on acne[7] and another study in which patients were fed large amounts of food that they believed exacerbated their acne,[8] we are not aware of any other published systematic study of the diet–acne relationship. The current consensus among dermatologists is to advise that patients avoid foods that they believe precipitate or worsen the condition.[5]

We examined data from the Nurses Health Study (NHS) II to evaluate the hypothesis that intake of dairy products is positively associated with risk of teenage acne. In addition, we examined other foods, such as french fries, pizza, and chocolate candy that have been hypothesized to be associated with teenage acne.[1,2] The study was approved by the Institutional Review Boards of the Brigham and Women's Hospital and the Harvard School of Public Health.

METHODS

Study population

The NHS II is an ongoing prospective cohort study designed to examine associations between lifestyle factors and the occurrence of diseases in women. It was established in 1989 when 116,671 female registered nurses aged 25 to 42 years and free of cancer responded to a baseline questionnaire. Follow-up questionnaires to ascertain lifestyle factors and occurrence of diseases have been mailed biennially since then and the follow-up rate exceeds 90%. In 1998, the members of the cohort were asked whether they would be willing to provide information about their high school diet. Some 47,355 participants responded and completed a high school diet food-frequency questionnaire. This analysis consists of women who completed the questionnaire and answered a question on physician-diagnosed severe teenage acne in 1989. Additional information about the study population was obtained from the relevant biennial questionnaire.

Semiquantitative food-frequency questionnaires and calculation of nutrient intake

The NHS II food-frequency questionnaire from which the high school food-frequency questionnaire was derived has been previously described, and the validity and reproducibility has been reported.[9,10] In brief, participants were asked how frequently on average they consumed the specified amount of food between the ages 13 and 18 years (eg, one 8-oz glass of milk or a carton). Nine responses are possible from never to more than 6 times a day. The responses for some of the food items were collapsed because of small cell sizes.

The dairy foods group included milk, instant breakfast drink, frappe (milkshakes), chocolate milk drink, sherbet, ice cream, yogurt, cottage cheese, cream cheese, other (hard) cheese, and butter. We also asked "between ages 13 and 18, what type of milk did you usually drink" and the response options were "whole milk," "powdered milk," "low-fat milk," "skim/nonfat milk," "don't know," and "didn't drink milk." Consumption of the specific types of milk was derived from the cross-classification of the responses to the usual type of milk consumed and the frequency of total milk consumption. We also examined other food items such as soda, french fries, pizza, and chocolate candy, some of which had been hypothesized to be associated with acne.[2,8]

Nutrient intakes were computed by multiplying the frequency of consumption of each unit of food and the nutrient content of the specified portions based on the nutrient values in foods obtained from US Department of Agriculture sources and food manufacturers, and then summing the contributions from all foods.[11] These were energy-adjusted by using the residuals from the regression of nutrient intake on total caloric intake.[12] Total calcium, and vitamins A and D intakes, were calculated from all sources, combining diet and supplements; dietary vitamin intakes were calculated from all dietary sources without supplements. The glycemic index values for foods in the questionnaire were obtained by testing food items at the nutrition center of the University of Toronto, or from published sources,[13] and the glycemic load was computed as previously described.[14]

The reproducibility of the high school diet questionnaire was validated in a subcohort of 228 participants who completed another questionnaire in 2002. The Pearson correlation coefficients were 0.67 for the dairy food group and 0.77 for milk.

Ascertainment of nondietary factors

Information about other possible risk factors such as age, height, body mass index (BMI) at age 18 years, and age at menarche was obtained from the biennial mailed questionnaires. For these variables, we used the data from the 1989 questionnaire or whenever such information was available in the updated questionnaires. We estimated BMI from weight

and height (kg/height in square meters) as a measure of total adiposity.

Identification of acne cases

In 1989, participants in the NHS II were asked "Have you ever had physician-diagnosed severe teenage acne?"

Statistical analysis

To assess the potential for selection bias, we compared acne history and categories of factors associated with history of acne among those women who completed the high school food-frequency questionnaire and those who did not using the Wilcoxon rank sum test for continuous variables and the chi-sqaure test for categoric variables. We computed prevalence ratios (PR)[15] using the log binomial likelihood. In multivariate analysis, we adjusted for energy intake (quintiles), age in 1989 (quintiles), age at onset of menarche (<12, 12, 13, >13 years), and BMI (<20, 20-22, 23-25, 26-30, >30 kg/m^2). The food items were modeled as categories of servings per week or per day. PR and 95% confidence interval (CI) were calculated for each category of intake and were compared with the lowest category of intake as the reference value. The lowest category of intake for types of milk included low intakes of all types of milk. In tests for linear trend, food intake was modeled as continuous variables of servings per day.

We categorized the energy-adjusted values of each nutrient into quintiles (except vitamin D from supplements, which was categorized into quartiles) and modeled the PR for each quintile with the lowest quintile as the reference category. In tests for linear trend across quintiles of nutrient intake, we assigned the median measured value to each category and used these values as a continuous variable. Missing value indicators were created for those with missing covariates because we had few missing data.[16,17] We present 2-sided 95% CIs for all PRs.

RESULTS

When they were adolescents, most women (61.2%) drank whole milk, whereas 20.2% drank low-fat milk, 7.4% skim milk, and 2.1% powdered milk. Only 7.7% did not drink milk and 1.4% did not indicate the type of milk that they usually drank. Women who did not report their high school diet had slightly lower prevalence of severe teenage acne (6.8% compared with 7.2%). Otherwise; there was no notable difference between the two groups with respect to age, BMI, and age at menarche.

Table I shows the age-standardized prevalence of the risk factors for acne according to total milk intake in the cohort. Energy, transunsaturated fat, saturated fat, total vitamin D, vitamin D from supplements, vitamin D from food, and calcium intake increased with increased intake of total milk.

In a model that included categories of skim milk intake, BMI at age 18 years, age in 1989, and age at onset of menarche, the multivariate PRs (95% CI, *P* value for test of trend) comparing the highest to the lowest category were 0.77 (0.60, 0.98; .06) for BMI at age 18 years, 0.76 (0.69, 0.84; <.001) for age at onset of menarche, and 0.89 (0.81, 0.99; .04) for age at baseline.

Foods

The reported prevalence of severe acne according to the intake of total milk was 0.06 for 1 or fewer serving/wk, 0.07 for 1 serving/wk, 0.07 for 2 to 4 servings/wk, 0.07 for 5 to 6 serving/wk, 0.07 for 1 serving/d, 0.08 for 2 to 3 serving/d, and 0.08 for more than 3 servings/d.

Table II shows the multivariate analyses for intake of types of milk adjusted for age at baseline and at onset of menarche, BMI at age 18 years, and energy intake. The multivariate PRs (95% CI; *P* value for test of trend) for women with the highest categories of intake (>3 servings/d for all types of milk combined and ≥2 servings/d for specific types of milk) compared with the lowest (≤1 serving/wk) were 1.22 (1.03, 1.44; .002) for total milk, 1.12 (1.00, 1.25; .56) for whole milk, 1.16 (1.01, 1.34; .25) for low-fat milk, and 1.44 (1.21, 1.72; .003) for skim milk.

For the other dairy foods and foods commonly associated with acne, there were significant positive associations with instant breakfast drink, sherbet, cream cheese, and cottage cheese. The multivariate PRs (95% CI; *P* value for test of trend) for the highest categories of intake (≥1 servings/d) compared with the lowest (≤1 serving/wk) were 1.46 (1.21, 1.77; .001) for instant breakfast drink, 1.28 (0.82, 1.99; .03) for sherbet, 1.63 (1.22, 2.20; .02) for cottage cheese, and 1.44 (0.98, 2.12; .03) for cream cheese. Other dairy foods, soda, french fries, chocolate candy, and pizza were not significantly associated with acne. In addition, we adjusted our estimate of the effect of milk intake by including saturated and trans-unsaturated fats in our multivariate models. The results remained materially unchanged.

Nutrients

PR (95% CI; *P* value for test of trend) adjusted for age at baseline and at onset of menarche, BMI at age 18 years, and energy intake for the highest quintile of nutrient intake compared to the lowest were 1.10 (1.00, 1.22; .001) for total vitamin D; 1.01 (0.91, 1.11; .05) for vitamin D from foods; 1.07 (0.96, 1.18; .02)

Table I. Age-standardized distribution of risk factors for acne by categories of total milk intake among the Nurses' Health Study II participants at baseline, 1989, United States

Servings (glasses)	<1/wk	1/wk	2-4/wk	5-6/wk	1/d	2-3/d	≥4/d
No.	6280	1816	5848	4544	8808	17,272	2310
Mean BMI at age 18 y, kg/m^2	21.3	21.4	21.3	21.3	21.3	21.1	21.1
Age at menarche, y	12.5	12.3	12.4	12.4	12.4	12.4	12.5
Calorie intake, kJ	10,016	10,238	10,669	11,088	11,318	12,276	13,883
Saturated fat, g	41.3	41.8	43.7	46.1	47.5	54.2	65.7
Transunsaturated fat, g	6.4	6.4	6.6	6.8	7.1	7.7	8.5
Total vitamin D, IU	198	207	245	291	305	462	683
Vitamin D from foods, IU	168	179	210	249	266	413	626
Vitamin D from supplements, IU	29.6	28.4	33.9	41.4	38.9	49.1	56.9
Calcium, mg	619	671	773	895	964	1416	2069

BMI, Body mass index.

for trans unsaturated fat; 0.88 (0.80, 0.98; .04) for saturated fat; 1.03 (0.93, 1.13; .04) for calcium; 0.95 (0.86, 1.05; .08) for total vitamin A; and 0.95 (0.86, 1.05; .79) for vitamin A from foods. In a similarly adjusted model, the PR (95% CI, *P* value for test of trend) comparing the highest to the lowest quartile of vitamin D from supplements intake was 1.22 (1.08, 1.37; .004). In a model adjusted for age at baseline, age at onset of menarche, and BMI at age 18 years only, the PR (95% CI, *P* value for test of trend) comparing the highest to the lowest quintile was 1.30 (1.17, 1.44; <.001) for energy intake (Table III).

Intakes of total, animal, vegetable, monounsaturated, polyunsaturated fats; cholesterol; and glycemic load were not associated with acne history (data not shown).

DISCUSSION

In this large cohort study of women, we found that intake of milk during adolescence was associated with history of teenage acne. This association was more marked for skim milk than for other forms of milk suggesting that the finding is unlikely to be caused by the fat content of milk. Instant breakfast drink, cream cheese, and cottage cheese were also associated with acne. These associations may be because of the milk content of these foods. In addition, there was weak inverse association with saturated fat and positive associations with transunsaturated fat and energy intake, which may be caused by chance. We found positive associations with total vitamin D and vitamin D from supplements, and relatively weaker positive associations with vitamin D from foods. The active metabolite of vitamin D, 1α, 25-dihydroxyvitamin D_3, plays an important role in epidermal differentiation by inhibiting the proliferation of keratinocytes while augmenting their differentiation.[18] It positively interacts with testosterone's actions in several organs systems.[19] Our result suggests that there may be an independent association with vitamin D intake from supplements. We also found positive associations with correlates of early sexual maturity such as BMI and age at onset of menarche, which is consistent with results of other studies.[20,21]

The role of diet in the development of acne has been controversial. Although there have been several case reports,[1,2] few systematic studies have been done. Fulton et al,[7] in a crossover single-blinded short-duration study of 65 patients, showed that there was no association between the consumption of chocolate bars and acne, sebum production and composition, and comedogenicity. Interestingly, the chocolate bars used in their studies had no milk component, in contrast to a typical chocolate bar of the period.[7] The perceived association with commercial chocolate products may, therefore, be a result of confounding by the presence of milk. In another study, patients were fed large amounts of food that they believed exacerbated their acne without any noticeable effect.[8] In contrast, Robinson[6] reported 1925 patients who kept food diaries and found that milk was the most common food implicated in acne flares.

We hypothesize that the hormonal content of milk may be responsible for the association with acne. Milk contains estrogens, progesterone, the androgen precursors androstenedione and dehydroepiandrosterone-sulfate, and 5α-reduced steroids like 5α-androstanedione, 5α-pregnanedione, and dihydrotestosterone, some of which have been implicated in comedogenesis.[22,23] Milk also contains bioactive molecules that act on the pilosebaceous unit such as glucocorticoids, insulin-like growth factor (IGF)-1, transforming growth factor-β (TGF-β), neutral thyrotropin-releasing hormone-like peptides, and opiate-like compounds,[24] some of which survive processing,[22] but their

Table II. Prevalence ratios and 95% confidence intervals for acne by categories of intakes of types of milk in the Nurses' Health Study II participants at baseline, 1998, United States

	Milk types							
Servings (glasses)	**<1/wk**	**1/wk**	**2-4/wk**	**5-6/wk**	**1/d**	**2-3/d**	**>3/d**	***P* value for test of trend**
Total milk								
Cases/total	408/6280	128/1816	394/5848	307/4545	638/8808	1344/17,272	193/2310	
Age-adjusted	1.00	1.08	1.04	1.04	1.11	1.20	1.29	<.001
PR 95% CI		(0.89, 1.31)	(0.91, 1.18)	(0.90, 1.20)	(0.99, 1.26)	(1.08, 1.34)	(1.10, 1.53)	
PR* 95% CI		1.08	1.03	1.03	1.10	1.16	1.22	.002
		(0.89, 1.31)	(0.90, 1.18)	(0.89, 1.19)	(0.97, 1.24)	(1.04, 1.30)	(1.03, 1.44)	

Servings (glasses)	**<1/wk**	**1-6/wk**	**1/d**	**>1/d**	***P* value for test of trend**
Whole milk					
Cases/total	408/6280	519/8201	411/5804	968/12,900	
Age-adjusted PR 95% CI	1.00	0.98 (0.86, 1.11)	1.10 (0.96, 1.25)	1.17 (1.04, 1.31)	.11
PR* 95% CI	1.00	0.97 (0.86, 1.10)	1.07 (0.94, 1.23)	1.12 (1.00, 1.25)	.56
Low-fat milk					
Cases/total	408/6280	202/2634	154/1945	352/4409	
Age-adjusted PR 95% CI	1.00	1.16 (0.98, 1.36)	1.20 (1.00, 1.43)	1.21 (1.05, 1.39)	.12
PR* 95% CI	1.00	1.15 (0.98, 1.36)	1.17 (0.98, 1.40)	1.16 (1.01, 1.34)	.25

Servings (glasses)	**<1/wk**	**1-6/wk**	**1/d**	**≥2/d**	***P* value for test of trend**
Skim milk					
Cases/total	408/6280	65/814	48/729	161/1669	
Age-adjusted PR 95% CI	1.00	1.22 (0.95, 1.56)	1.00 (0.75, 1.34)	1.48 (1.24, 1.76)	.004
PR* 95% CI	1.00	1.23 (0.96, 1.58)	0.99 (0.74, 1.33)	1.44 (1.21, 1.72)	.003

CI, Confidence interval; *PR*, prevalence ratio.
*Multivariate PR for categories of intake, adjusted for age at baseline and at menarche, body mass index at age 18 y, and calorie intake.

detailed biochemistry, transport, and metabolism is not known.

Most studies of the hormonal content of milk have focused on progesterone but there are some reports about androgens. The reported testosterone concentration in milk ranges from 0.02 to 0.15 $\mu g/L$,[1,25,26] whereas that of androstenedione ranges from 0.1 to 3.5 $\mu g/L$[1,26] depending on the state of pregnancy of the cow. How processing affects the levels of these hormones is not well understood, but additional testosterone production from precursors like androstenedione and estrone occurs in dairy products like cheese during the fermentation phase.[22]

The estimated daily intake of testosterone from milk in German prepubertal girls was 0.02 $\mu g/d^{-1}$, representing 30% to 40% of daily intake from food sources, whereas that of dehydroepiandrosterone was 0.06 $\mu g/d^{-1}$, approximately 10% to 15% of daily dietary intake. This was thought to be small compared with a mean daily testosterone production in the same population of 32 $\mu g/d^{-1}$. In addition, even these estimated dietary intakes would be reduced further by first pass metabolism in the liver.[22] However, doubt has been cast on the sensitivity of the assay systems used to measure low levels of sex steroids, and the methodology used to compute the daily production rates of hormones.[27] Previous methods were based on metabolic clearance rates extrapolated from adult studies that did not adequately account for the difference in body surface area, binding capacity of the serum transport hormones, and the metabolizing capacity of the liver, all of which differ significantly between adults and children. Recent assay techniques suggest that the

Table III. Prevalence ratio, 95% confidence intervals for acne by quintiles of high school nutrient intake (energy-adjusted, except for energy intake) in the Nurses' Health Study II, 1998, United States

	Nutrients					
Quintiles	1 (Lowest)	2	3	4	5	*P* value for test of trend
Calories						
Median, kJ	7456	9547	11,196	13,046	16,037	
Cases/total	548/9186	650/9203	638/9179	705/9186	775/9194	
PR*† 95% CI	1.00	1.10 (0.99, 1.22)	1.08 (0.97, 1.20)	1.19 (1.07, 1.31)	1.30 (1.18, 1.44)	<.001
Total vitamin A						
Median, IU	5904	8539	10,876	14,218	21,056	
Cases/total	639/9191	658/9187	670/9191	704/9188	645/9191	
PR* 95% CI	1.00	0.97 (0.88, 1.08)	1.00 (0.90, 1.10)	1.03 (0.94, 1.14)	0.95 (0.86, 1.05)	.80
Vitamin A from foods						
Median, IU	5762	8234	10,375	13,460	20,103	
Cases/total	650/9187	667/9191	648/9191	695/9190	656/9189	
PR* 95% CI	1.00	0.97 (0.88, 1.07)	0.95 (0.86, 1.05)	1.01 (0.91, 1.11)	0.95 (0.86, 1.05)	.79
Total vitamin D						
Median, IU	159.7	236.9	324.2	410.6	590.9	
Cases/total	610/9185	649/9195	648/9186	697/9194	712/9188	
PR* 95% CI	1.00	0.99 (0.90, 1.10)	0.96 (0.87, 1.06)	1.07 (0.97, 1.18)	1.10 (1.00, 1.22)	.001
Vitamin D from foods						
Median, mg	153.9	223.5	297.6	372.6	483.8	
Cases/total	648/9193	620/9184	686/9191	687/9189	675/9191	
PR* 95% CI	1.00	0.90 (0.82, 1.00)	0.97 (0.88, 1.07)	1.00 (0.90, 1.10)	1.01 (0.91, 1.11)	.05
Quartiles						
Vit. D from supplements						
Median, mg	0	56	228	400		
Cases/total	2698/35,941	122/1238	212/2513	284/2940		
PR* 95% CI	1.00	1.23 (1.04, 1.47)	1.07 (0.93, 1.22)	1.22 (1.08, 1.37)		.004
Qintiles						
Calcium						
Median, mg	677	867	1048	1265	1558	
Cases/total	667/9209	621/9148	646/9229	668/9166	714/9196	
PR* 95% CI	1.00	0.88 (0.79, 0.97)	0.89 (0.81, 0.98)	0.92 (0.84, 1.02)	1.03 (0.93, 1.13)	.04
Transunsaturated fat						
Median, g	4.56	5.86	6.95	8.13	9.99	
Cases/total	613/9197	654/9141	677/9200	664/9216	708/9194	
PR* 95% CI	1.00	0.99 (0.89, 1.09)	1.01 (0.91, 1.12)	0.98 (0.89, 1.09)	1.07 (0.96, 1.18)	.02
Saturated fat						
Median, g	39.6	45.1	48.9	52.9	58.9	
Cases/total	711/9187	692/9195	684/9186	593/9197	636/9183	
PR* 95% CI	1.00	0.93 (0.84, 1.02)	0.92 (0.83, 1.01)	0.80 (0.72, 0.89)	0.88 (0.80, 0.98)	.04

CI, Confidence interval; *PR*, prevalence ratio.
*Multivariate PR for categories of intake, adjusted for age at baseline and at menarche, body mass index at age 18 y, and energy intake.
†Calories adjusted for age at baseline, body mass index at age 18 y, and age at onset of menarche.

sex steroid levels in prepubertal children may be much lower than previous estimates, but the actual values are unsettled.[28]

Milk intake has also been associated with increased plasma IGF-1 levels[29-31] and may be related to acne through this pathway. Although some absorption of dietary milk-borne IGF-1 occurs in neonatal rats, the same has not been demonstrated in human beings. Elevated plasma IGF-1 may result from an endogenous response to milk intake.[29-31] Human and bovine IGF-1 share the same amino acid sequences[32] and several milk proteins protect IGF-1 from digestion in the gut.[33] IGF-1 may mediate some of the effects of comedogenic factors, like androgens, growth hormone, and glucocorticoids.[34] In human studies, exogenous androgens increase serum IGF-1

levels and vice versa.[35] High serum IGF-1 and androgen levels have been reported in patients with adult acne[36] and elevated serum dehydroepiandrosterone-sulfate positively correlates with acne in prepubertal girls.[20] Sebum production increases in response to both androgens and IGF-1.[4,34]

Because the association between milk intake and acne was strongest and clearest for skim milk, our findings suggest that the bioavailability of the responsible factor or factors might be increased during production of skim milk. We speculate that skim milk processing may have altered the relative bioavailability of bioactive molecules or their interactions with binding proteins. Alternatively, whole milk contains more estrogen than skim milk[37] and estrogens tend to reduce acne. It is possible that the balance of hormonal constituents of skim milk has been altered, rendering it more comedogenic.

Whey proteins are thought to be the primary transport proteins in milk.[38] In addition, they have intrinsic biologic functions.[38] α-Lactalbumin, one of the major whey proteins, undergoes pressure-induced conformational alteration that leads to changes in biologic function.[39] In addition, animals fed α-lactalbumin-enriched whey protein show increased will and capacity to engage in physical activities, gained lean body mass, improved efficiency of exercise training, and decreased percentage body fat mass compared with those fed whole milk enriched diet; all of which are similar to the effect of androgens.[40,41] In addition, whey proteins are added to low-fat and skim milk to simulate the consistency of whole milk. These added proteins, specifically α-lactalbumin, might, therefore, play a role in comedogenesis, either directly or as carriers of bioactive molecules. These pathways, and perhaps others, may be involved in acne and other hormonally dependent disease processes in women, especially breast cancer because the mammary gland shares close evolutionary and embryologic relationship with sebocytes.[42,43]

For this analysis, we studied only those women who completed a high school diet food-frequency questionnaire; 41% of our cohort participants. Although this could have introduced selection bias in addition to those biases to which cross-sectional studies are prone,[44] women who did not report their high school diet had slightly lower prevalence of acne than those who did but were otherwise similar. It is possible that there are other reasons for nonresponse to the food-frequency questionnaire that may be related to either the exposure or the outcome variables. For example, if those who had unpleasant high school experiences because of severe acne choose not to complete the high school food-frequency questionnaire, our study will be biased toward the null. However, our data did not support this suggestion. There may also be a relationship between milk intake and the likelihood that a study participant will consult a physician for acne that we have not accounted for in this study. Selection bias is unlikely when the two groups are so similar with respect to key features of acne. In addition, though we have shown that our participants' recall of their high school diet is highly reproducible, recall of diet so distant in the past may be imprecise.[45] The consumption of low-fat milk in the United States continued to increase during the period covered by this study and did not gain widespread acceptance until the late 1980s.[46] In addition, states in the United States had differing definitions for types of milk during the period covered by this study; therefore, we may not have distinguished the types of milk intakes well.

We cannot rule out reverse causation in a cross-sectional analysis such as this. Because an association between dairy products and acne was not well known, this is not likely to be a significant problem in this study and, if anything, would tend to produce an inverse association if adolescents avoided milk because of acne. On the hand, if our participants had abandoned soda for milk, we would in addition have found an inverse association with soda, but this was not so in this study. Nondifferential error in recall may bias the association toward the null and reduce the strength of the association. This error is likely to be greater in a recall of high school diet compared with the usual food-frequency questionnaire that seeks information about diet in the past year. Many of our participants were misclassified as not having acne because we asked about physician-diagnosed severe teenage acne, and the reported prevalence greatly underestimates the total occurrence of acne. Significant misclassification of acne prevalence may also reduce the strength of association between acne and milk intakes.

In conclusion, we found that intake of milk was associated with increased risk of teenage acne in girls. This finding suggests that the hormonal constituents of milk are present in sufficient quantities to have biologic effects in girls, and raises the possibility that other hormonally sensitive glands may also be affected. Because of the potential importance for acne and possibly breast cancer, these relationships should be evaluated further.

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