

## REVIEW

## Diet and acne

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Historically, the relationship between diet and acne has been highly controversial. Before the 1960s, certain foods were thought to exacerbate acne. However, subsequent studies dispelled these alleged associations as myth for almost half a century. Several studies during the last decade have prompted dermatologists to revisit the potential link between diet and acne. This article critically reviews the literature and discusses how dermatologists might address diet when counseling patients with acne. Dermatologists can no longer dismiss the association between diet and acne. Compelling evidence exists that high glycemic load diets may exacerbate acne. Dairy ingestion appears to be weakly associated with acne, and the roles of omega-3 fatty acids, antioxidants, zinc, vitamin A, and dietary fiber remain to be elucidated. This study was limited by the lack of randomized controlled trials in the literature. We hope that this review will encourage others to explore the effects of diet on acne. (J Am Acad Dermatol 10.1016/j.jaad.2009.07.043.)

**Key words:** acne; dairy; diet; glycemic index; glycemic load; nutrition; omega-3 fatty acids; vitamin A; vitamins; zinc.

**H**istorically, the relationship between diet and acne has been highly controversial. In the 1930s through 1960s, patients were often discouraged from eating a wide selection of foods including chocolate, fats, and sweets. Following a few critical studies,<sup>1,2</sup> these alleged associations between foods and acne were dispelled as myth for almost half a century. Consequently, dietary restrictions have not been recommended as a standard part of acne therapy for decades. Recently, however, the relationship between diet and acne has been called back into question. Several carefully designed and thought-provoking studies during the last decade have prompted dermatologists and nutritionists to revisit the alleged link between diet and acne. In particular, evidence that the ingestion of certain dairy products, carbohydrates, or both may exacerbate acne has been particularly compelling and merits examination. A comprehensive review of the literature to date follows, with particular attention

*Abbreviations used:*

BMI:	body mass index
DHT:	dihydrotestosterone
GI:	glycemic index
HGL:	high glycemic load
IGF:	insulin-like growth factor
IGFBP:	insulin-like growth factor binding protein
LGL:	low glycemic load

paid to the influence of dairy products and carbohydrate intake on acne severity. Although the majority of evidence supporting a link between diet and acne falls under one of these two categories, a brief discussion of other dietary factors implicated in acne including omega-3 fatty acids, antioxidants, zinc, vitamin A, and iodine follows. Very few, if any, human data are available to support a role for these factors in acne, but some in vitro and animal data exist. Prospective controlled trials, prospective and retrospective cohort studies, case-control studies, and large case series examining the role of diet in acne, published in the English language and available on PubMed, were included in this review (Table I). We have included several studies that we believe are of inferior design in an effort to provide historical context for more recent developments, and to address several dietary factors that, in our opinion, merit further study.

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## DIET AND ACNE: A HISTORICAL FRAMEWORK

Before the 1960s, dietary advice was a standard part of acne therapy. Data published in 1931

suggested that impaired glucose tolerance existed in patients with acne.<sup>3</sup> Abnormal carbohydrate metabolism was implicated in acne and patients were recommended to avoid consuming excessive carbohydrates and high-sugar foods.<sup>4</sup> Major textbooks of dermatology<sup>5-7</sup> popular in the 1940s and 1950s perpetuated these beliefs and discouraged foods such as chocolate, fats, sweets, and carbonated beverages as part of acne therapy. However, the contention that a relationship existed between diet and acne was abandoned after the following two studies showed no association.

### EARLIER STUDIES THAT SHOWED NO ASSOCIATION BETWEEN DIET AND ACNE

In 1969, Fulton et al<sup>1</sup> investigated the effect of chocolate on acne vulgaris in a crossover single-blinded study. A total of 65 subjects were assigned to eat either a chocolate bar or a control bar with similar appearance and caloric content. Subjects ate the assigned bar daily for 4 weeks and then after a 3-week rest period, consumed the alternate bar for 4 weeks. Acne was scored as worsened or improved if the total number of lesions increased or decreased by 30%, respectively. The authors found that acne severity did not change during the chocolate bar and control bar study periods and concluded that chocolate did not affect the course of acne. However, this study was flawed for several reasons. The duration of the study was far too short for the chosen outcome because most acne clinical trials last 12 weeks<sup>8-10</sup> to allow for the natural history of comedo formation and evolution. Furthermore, the placebo bar was an inappropriate control because it had similar total sugar and total fat content as the chocolate bar.<sup>11</sup> Moreover, the control bar was largely composed of partially hydrogenated vegetable oil rather than cocoa butter and cacao paste, the former of which contains high quantities of trans-fatty acids that contribute to inflammation.<sup>12,13</sup> Finally, most patients with dietary acne triggers report pustular flares rather than comedonal acne.<sup>14</sup> Fulton et al<sup>1</sup> grouped all acne lesions together. Thus, if a patient's acne lesions shifted from a comedonal to pustular predominance whereas the total number of lesions remained the same, this would have been scored as unchanged even though a clinically significant change would have been present.

In 1971, Anderson<sup>2</sup> also challenged the acne and diet association by assigning 27 students with reported history of dietary acne triggers to consume chocolate, milk, roasted peanuts, or cola for 1 week under direct supervision. The author did not specify how many of the 27 subjects were subdivided into each group. Before and after the trial, each subject's

acne lesions were mapped onto a sheet held over the face. Anderson<sup>2</sup> found that the foods produced no flares of acne. However, lesion counts were not reported and statistical analysis was not performed.<sup>15</sup> Furthermore, it is unlikely that any group had enough statistical power to provide significant results, given that the 27 patients were subdivided into 4 treatment categories. This study suffered from many limitations including small sample size

and lack of controls, blinding, and randomization.<sup>11,12</sup>

Finally, the studies by Fulton et al<sup>1</sup> and Anderson<sup>2</sup> have both been critiqued for their failure to take into consideration subjects' baseline diets, resulting in an inability to determine if the treatment diet varied from the subjects' normal diet.<sup>12,13,15</sup> This oversight may have obscured the study results.

### MORE MODERN STUDIES REVISIT THE LINK BETWEEN ACNE AND DIET: AN EXAMINATION OF THE INFLUENCE OF DAIRY PRODUCTS ON ACNE SEVERITY

The studies by Fulton et al<sup>1</sup> and Anderson,<sup>2</sup> although suffering from major design flaws, were sufficient to dissociate diet from acne in the minds of most dermatologists. Textbooks were revised to reflect this new academic consensus, and dermatologists took the stance that any mumblings about the association between diet and acne were unscientific and one of the many myths surrounding this ubiquitous disease.

Two decades before the studies of Fulton et al<sup>1</sup> and Anderson,<sup>2</sup> Robinson<sup>16</sup> took note of what he believed to be an association between dairy intake and acne severity. He documented that, based on 1925 subjects who kept strict food diaries, milk was the most commonly implicated food in acne flares. However, Robinson<sup>16</sup> failed to provide summary statistics and statistical analyses. His report is merely anecdotal and descriptive, based on his experience.

### CAPSULE SUMMARY

- Dermatologists can no longer dismiss the association between diet and acne.
- There is reasonably compelling evidence that high glycemic load diets may exacerbate acne.
- An association between dairy ingestion and acne may exist, but evidence is weak.
- The role of omega-3 fatty acids, antioxidants, zinc, vitamin A, and dietary fiber in acne is unclear.

**Table I.** Studies investigating relationship between diet and acne

Study	Design	Level of evidence	Subjects	Sample size	Intervention	Conclusions and limitations
Robinson, <sup>16</sup> 1949	Case series	2	Subjects with acne	1925	Diet diary	Milk was most commonly implicated food in acne flares. Limitations include short study duration of 1-2 wk and absence of data and statistical analysis.
Grant and Anderson, <sup>106</sup> 1965	Case series	3	Subjects with acne	8	Milk chocolate bar for 5 d; half of subjects consumed antacid before chocolate	Chocolate did not aggravate acne. Antacid did not affect results. Limitations include small sample size, short study duration, lack of control, lack of randomization, lack of blinding, and lack of consideration of subjects' baseline diets.
Bett et al, <sup>107</sup> 1967	Cross-sectional survey	3	Subjects with acne, control subjects with warts, and sex- and age-matched healthy control subjects	16 Subjects with acne, 16 control subjects with warts, 16 healthy control subjects	Questionnaire	Subjects with acne did not consume more sugar than control subjects. Limitations include small sample size and lack of validated questionnaire.
Fulton et al, <sup>1</sup> 1969	Crossover, subject-blind interventional study	1	Adolescents with acne and adult male prisoners with acne	30 Adolescents, 35 prisoners	Chocolate bar or control bar with similar caloric composition	Severity of acne did not change during chocolate bar and control bar study periods. Chocolate does not affect acne. Limitations include small sample size, short study duration, similar amounts of sugar and fat in both bars, inappropriate grouping, and lack of consideration of subjects' baseline diets.
Anderson, <sup>2</sup> 1971	Case series	3	University students who reported dietary acne triggers	27	Daily consumption of chocolate, milk, roasted peanuts, or cola for 1 wk	Study foods did not produce any acne flares. Limitations include small sample size, lack of control, lack of randomization, lack of blinding, absence of lesion counts, lack of statistical analysis, and failure to consider subjects' prestudy diets.

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**Table I.** Cont'd

Study	Design	Level of evidence	Subjects	Sample size	Intervention	Conclusions and limitations
Kligman et al, <sup>98</sup> 1981	Case series	2	Part 1: subjects with inflammatory acne Part 2: men with acne	Part 1: 136 Part 2: 39	Part 1: daily vitamin A 300,000 IU for 3-4 mo Part 2: either daily vitamin A 300,000 IU for 12 wk or daily vitamin A 300,000 IU for 1 wk followed by 400,000 IU for second wk and then 500,000 IU for next 10 wk	Retinol is effective treatment for acne at doses of 300,000 U for women and 400,000-500,000 U for men. Toxicity is minimal and limited mainly to xerosis and cheilitis. Limitations include lack of control, lack of randomization, lack of blinding, and lack of data on higher doses of vitamin A in women. Women were given oral contraceptives that may have confounded results.
Aizawa and Niimura, <sup>45</sup> 1996	Cross-sectional	3	Women with acne and age-matched control subjects	30 Subjects with acne, 13 control subjects	OGTT	Mild insulin resistance occurs during OGTT, however, postprandial hyperinsulinemia does not determine hyperandrogenemia in patients with acne. Limitations include small sample size and lack of generalizability beyond eumenorrheic women.
Dreno et al, <sup>89</sup> 2001	RCT, double-blind	1	Subjects with inflammatory acne	332	3 mo of Either elemental zinc 30 mg daily or minocycline 100 mg daily	Zinc and minocycline are both effective in treatment of inflammatory acne, however, minocycline has superior effect.
Cordain et al, <sup>37</sup> 2002	Cross-sectional	2	Kitavan of Papua New Guinea and Aché of Paraguay	1200 Kitavan, 115 Aché	Skin examination	No acne was observed in any subject. Difference in prevalence of acne between Western vs Kitavan and Aché societies may be partly caused by environmental factors such as diet. LGL diets may reduce acne. However, these isolated subcultures may have genetic and other environmental factors that account for absence of acne.
Chiu et al, <sup>108</sup> 2003	Prospective cohort	2	University students with acne	22	Subject-perceived diet quality	Worsening perceived diet quality is positively associated with acne. Limitations include small sample size and use of tool that has not been validated for measuring diet quality.

Adebamowo et al, <sup>17</sup> 2005	Retrospective cohort	2	Women	47,355	Food frequency questionnaire of distant dietary intake and subject report of physician-diagnosed severe acne	Acne is positively associated with intake of milk (particularly skim milk), instant breakfast drink, sherbet, and cottage cheese. Association between acne and dairy may be caused by hormones and bioactive molecules present in milk. These factors may be more bioavailable in skim milk. Limitations of this study include its retrospective design, loosely described definition of acne, subjects' imprecise recall of diet, failure to control for heredity and socioeconomic status, and low clinical significance of findings.
Adebamowo et al, <sup>34</sup> 2006	Prospective cohort	2	Girls aged 9-15 y at baseline	6094	Food frequency questionnaire	Acne is positively associated with intake of milk (particularly skim milk). Limitations include lack of validation of subjects' self-report of acne, low clinical relevance of findings, and failure to account for lack of trend between whole or low-fat milk with acne.
Smith et al, <sup>49</sup> 2007	RCT, investigator-blind	1	Male patients aged 15-25 y with acne	43	LGL diet or conventional HGL diet (control)	Patients on LGL diet had decreased total acne lesions, decreased weight, decreased free androgen index, and increased IGFBP-1 compared with control subjects. Major limitation is that independent effects of weight loss and dietary intervention were not isolated. Furthermore, study did not account for possible differences in dietary fat and fiber intake between two groups. Finally, it is difficult to generalize results of this study to women who undergo cyclical hormonal changes that may influence acne.

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**Table I.** Cont'd

Study	Design	Level of evidence	Subjects	Sample size	Intervention	Conclusions and limitations
Kaymak et al, <sup>46</sup> 2007	Cross-sectional	3	University students with acne and age- and sex-matched control subjects	49 Subjects with acne, 42 control subjects	Food frequency questionnaire	Dietary glycemic index, glycemic load, and insulin levels were similar in patients with acne compared with control subjects. These factors may not be involved in pathogenesis of acne in younger patients. Study limitations include lack of validated questionnaire, failure to provide copy of questionnaire, questionable timing of insulin level measurements, and failure to account for significant differences in IGF-1 and IGFBP-3 between acne and control groups.
Smith et al, <sup>48</sup> 2007	RCT, investigator-blind	1	Male patients aged 15-25 y with acne	43	LGL diet or carbohydrate-dense diet (control)	Patients on LGL diet had decreased acne lesions, decreased weight, decreased BMI, and increased insulin sensitivity compared with control subjects. Major limitation is that independent effects of weight loss and dietary intervention were not isolated. Furthermore, study did not account for possible differences in dietary fat and fiber intake between two groups. Finally, it is difficult to generalize results of this study to women who undergo cyclical hormonal changes that may influence acne.
Adebamowo et al, <sup>21</sup> 2008	Prospective cohort	2	Boys aged 9-15 y at baseline	4273	Food frequency questionnaire	Acne is positively associated with intake of skim milk. Milk may influence comedogenesis through hormonal pathways. Limitations include lack of validation of subjects' self-report of acne and failure to account for lack of trend between whole or low-fat milk with acne.

Smith et al, <sup>50</sup> 2008	Nonrandomized clinical trial	1	Male patients aged 15-20 y with acne	12	7-d Admission to research facility, controlled feeding of LGL or HGL diet	IGFBP-1 and IGFBP-3 increased from baseline in LGL group, whereas SHBG decreased from baseline in HGL group. Increased glycemic load may result in increased activity of sex hormones and IGF-1, thereby contributing to acne development. Limitations include small sample size, lack of randomization, and inability to generalize to female adolescents.
Smith et al, <sup>51</sup> 2008	RCT	1	Male patients aged 15-25 y with acne	31	LGL diet or control diet	Compared with control group, LGL group had increased ratio of skin surface SFAs to MUFAs. This increased ratio was negatively associated with number of acne lesions. Increased follicular sebum outflow was also correlated with increased proportion of sebum MUFAs. Limitations include failure to account for confounding effect of weight loss in LGL group, lack of standards to ensure compliance with specified diet, and inability to generalize to female patients or subjects outside of 15- to 25-y age range.
Rouhani et al, <sup>56</sup> 2009	Cross-sectional	2	Subjects adhering to low-glycemic South Beach diet	2528	World Wide Web-based questionnaire	Subjects reported improvement of acne and reduction of acne treatment while adhering to low-glycemic South Beach diet. Limitations include lack of validation of subjects' self-report of acne, presence of confounding factors such as weight loss and exercise, recall bias, and selection bias.

*BMI*, Body mass index; *HGL*, high glycemic load; *IGF*, insulin-like growth factor; *IGFBP*, insulin-like growth factor binding protein; *LGL*, low glycemic load; *MUFA*, monounsaturated fatty acid; *OGTT*, oral glucose tolerance test; *RCT*, randomized controlled trial; *SFA*, saturated fatty acid; *SHBG*, sex hormone-binding globulin.

Key to level of evidence: (1) prospective controlled trial; (2) retrospective study, prospective cohort study, large cross-sectional study, or large case series; (3) small cross-sectional study, small case series, or individual case reports.

In 2005, Adebamowo et al<sup>17</sup> re-examined this alleged connection between dairy and acne. A total of 47,355 adult women were asked to recall their high school diet using a validated food frequency questionnaire. Subjects were also asked if they ever had physician-diagnosed severe acne. The authors found that acne was positively associated with reported quantity of milk ingested, particularly skim milk.

The authors speculated that dairy influences acne through hormonal mediators and by increasing plasma insulin-like growth factor (IGF)-1 levels. With regard to hormonal effects of milk, it is known that milk contains the testosterone precursors androstenedione and dehydroepiandrosterone-sulfate.<sup>18</sup> In vivo, endogenous testosterone is converted via 5 $\alpha$ -reductase to dihydrotestosterone (DHT), which stimulates the pilosebaceous unit. However, DHT can be produced without 5 $\alpha$ -reductase in the setting of exogenous 5 $\alpha$ -reduced molecules.<sup>19</sup> Milk contains 5 $\alpha$ -reduced steroids, notably 5 $\alpha$ -androstenedione and 5 $\alpha$ -pregnenedione, which are DHT precursors.<sup>18</sup> Both testosterone precursors and 5 $\alpha$ -reduced molecules are thought to contribute to the comedogenicity of milk<sup>17,18,20</sup> by stimulating sebum production and hyperkeratinization of the pilosebaceous unit.

It has been proposed that milk also increases comedogenicity through interactions with the IGF-1 pathway.<sup>21</sup> Milk, particularly skim milk, is positively correlated with higher plasma IGF-1 levels.<sup>22-24</sup> IGF-1 stimulates synthesis of androgens in both ovarian<sup>25</sup> and testicular<sup>26</sup> tissues and inhibits hepatic synthesis of sex hormone-binding globulin<sup>27</sup> resulting in increased bioavailability of androgens.<sup>15</sup> Both IGF-1<sup>28</sup> and androgens<sup>29,30</sup> increase sebum production, which is implicated in acne.

When broken down into categories of milk type, including whole, low fat, and skim, Adebamowo et al<sup>17</sup> found that only skim milk showed a statistical correlation with acne. This may be surprising given that one might expect bovine hormones to be concentrated in the lipid fraction of milk.<sup>31</sup> The authors hypothesized that the bioavailability of the factors responsible for comedogenicity of milk may be increased by skim milk processing.<sup>17</sup> They also postulated that skim milk is more acnegenic because, in comparison with whole milk, skim milk contains less estrogen, a hormone known to reduce acne.<sup>17</sup> It is unknown how processing affects hormone levels but it has been documented that fermentation that occurs with cheese production results in additional testosterone production from androgen precursors.<sup>20</sup> Because the association between milk and acne was more marked for skim milk, it was

postulated that the fat content of milk itself was unlikely correlated to comedogenicity. In the study of Adebamowo et al,<sup>17</sup> there were also positive associations found between acne and instant breakfast drink, sherbet, and cottage cheese. These associations were attributed to the milk content of the foods.

This study had several limitations, notably its retrospective design. Adult women were asked to recall their high school dietary intakes. Patients' recollection of their milk consumption in the distant past may have been imprecise.<sup>17</sup> Women were also asked to recall if they ever had physician-diagnosed severe acne. The word "severe" is subjective and patients may not have known how their physicians graded acne. Another drawback of this study was that it did not control for confounding variables such as heredity, nationality, and socioeconomic background.<sup>32</sup> Specifically, the study has been criticized for failing to account for the possibility that the iodine content of milk might be contributing to the apparent association between milk and acne.<sup>33</sup> Finally, the clinical significance of the results has been called into question. The percent of patients who remembered having physician-diagnosed acne was 6% for those who drank less than one glass of milk per week and 8% for those who drank more than 3 glasses of milk per day.<sup>32</sup> In a study with enough power, such as this 47,355 member cohort, it is relatively easy to show a statistically significant association between two variables. However, the incrementally increased prevalence of acne in those who consumed higher amounts of milk may not have been clinically significant. This study might also have been subject to information bias. The cohort studied attended high school between the 1960s and 1990s. During these years, although the medical community began to view the link between diet and acne as myth, this information did not immediately disseminate to the public. Therefore, sweet foods and beverages such as soda were often avoided, even during the 1960s through 1980s, by those who had acne in an attempt to ameliorate their disease. If these subjects were actively avoiding soda, they might have been more likely to consume milk.

In 2006, Adebamowo et al<sup>34</sup> set out to uphold their previous findings, this time using a prospective study design. The researchers examined 6094 girls aged 9 to 15 years at baseline who were prospectively followed up for up to 3 years. Subjects completed validated food frequency questionnaires and self-reported the frequency and amount of pimples they experienced. Positive associations were found between prevalence of acne



and intake of total milk, whole milk, low-fat milk, and skim milk. These trends were significant even when girls using oral contraceptives and girls aged 11 years or older were each excluded. Like the previous study, there was also no association between dairy fat and acne. The advantage of this study was its prospective design. However, this study was limited by the lack of validation of the subjects' self-report of acne. Severity of acne as assessed by a physician does not always correlate with self-report of acne. A recent study measuring the validity of self-report for acne showed that college students cannot accurately report that they have acne.<sup>35</sup>

Again, although statistically significant, the prevalence ratios demonstrating an association between milk and acne were very low (maximum of 1.24). Thus, the clinical relevance of these results remains in question. In 2008, Adebamowo et al<sup>21</sup> demonstrated similar results in a cohort of 4237 boys followed up prospectively. Like the adolescent girls, these boys all completed food frequency questionnaires and were asked about their pimples. There was a positive association between intake of skim milk and prevalence of acne. The multivariate prevalence ratio of acne adjusted for age, height, and energy intake was 1.19 (95% confidence interval 1.01-1.40,  $P$  value < .02) for those who consumed skim milk more than twice a day compared with those who consumed less than one serving per week of skim milk. Aside from this single weak association, this study did not find a significant association between total milk consumption and acne. There was also no association between acne with total fat, dairy fat, nor vitamin A and thus these compounds were not thought to contribute to the acnegenic properties of milk.

This trial did have the advantage of a prospective design. However, once again, the authors did not account for the fact that there was no significant trend between intake of whole or low-fat milk with acne.<sup>31</sup> As stated previously, bovine hormones would likely be concentrated in the lipid fractions of milk, making this repeated lack of association between fattier milks and acne perplexing.<sup>31</sup> However, it is theoretically possible that the findings may be a result of differences in the glycemic load of full versus skim milk. For a 250-g serving size, the glycemic load of full-fat milk has been reported to be 3 whereas the glycemic load of skim milk is 4.<sup>36</sup> The nearly equivalent glycemic loads of skim milk and full-fat milk can hardly explain the latter's stronger association with acne.

Drawbacks of all the dairy studies by Adebamowo et al<sup>17,21,34</sup> were that they were based on subjects' self-

reports rather than objective measures. In addition, they were all observational as opposed to randomized, controlled trials. Lastly, the associations that were detected were all weak by epidemiologic standards in that the odds ratios of associations were consistently close to 1. However, the authors did demonstrate an association between milk and acne in 3 separate populations, and thus, further investigation through randomized controlled trials is warranted.

### **MORE MODERN STUDIES REVISIT THE LINK BETWEEN ACNE AND DIET: AN EXAMINATION OF THE INFLUENCE OF CARBOHYDRATE INTAKE ON ACNE SEVERITY**

Although those mentioned above were working out the link between dairy and acne, others were focusing on the potential association between carbohydrate ingestion and acne severity. In 2002, Cordain et al<sup>37</sup> performed a cross-sectional study in which 1300 subjects from two non-Westernized societies, the Kitavan Islanders of Papua New Guinea and the Aché hunter-gatherers of Paraguay, underwent skin examination by a general practitioner trained in the detection and diagnosis of acne. Among these subjects, no cases of acne were reported. Cordain et al<sup>37</sup> suggested that the absence of acne in these societies may have been a direct consequence of their diets. The Kitavans and Achés subsist on low glycemic load (LGL) diets, devoid of Western refined foods such as cereals, chips, cookies, and bread.

The glycemic index (GI), developed in 1981, is a relative comparison of the potential of various foods to increase blood glucose based on equal amounts of carbohydrates in the food.<sup>38</sup> The concept of glycemic load was developed in 1997, and is calculated by multiplying the GI times the carbohydrate content/serving size.<sup>39</sup> In effect, the glycemic load takes into account both the quality and quantity of carbohydrates ingested. Dietary glycemic load is a measure of the blood glucose- and insulin-increasing potential, as it represents both the rate of carbohydrate absorption (the GI) and the quantity of carbohydrate consumed.<sup>40</sup> Examples of low- and high-glycemic foods can be found in [Table II](#).

In a subsequent review article, Cordain et al<sup>41</sup> postulated that diet-induced hyperinsulinemia leads to a cascade of endocrine responses that may influence the development of acne through androgens, IGF-1, IGF binding protein (IGFBP)-3, and retinoid signaling pathways. The authors purport that a hyperinsulinemic diet acts as a risk factor in the development of acne through influences on follicular epithelial growth, keratinization, and androgen-mediated sebum secretion.

**Table II.** Examples of low- and high-glycemic foods<sup>36</sup>

Food	Glycemic index*	Glycemic load <sup>†</sup> (per 100-g serving)
Carrots, raw	16	1.6
Peanuts	14	1.7
Oranges, raw	42	3.9
Plums, raw	39	3.9
Apples, raw	38	4.8
Porridge made from rolled oats	58	5.1
Chickpeas, boiled	28	5.6
Spaghetti, white, boiled	42	11.0
White flour bread	70	32.7

\*Listed glycemic index is when glucose sugar is used as reference food.

<sup>†</sup>Adapted from Foster-Powell et al.<sup>36</sup> Glycemic load is estimated by multiplying glycemic index by grams of carbohydrate per 100-g serving and dividing by 100.

The proposition of Cordain et al,<sup>37</sup> linking the absence of acne in the Kitavan and Aché to a single variable such as dietary GI, although intriguing, has been heavily criticized. Not only do these isolated subcultures have similar diets, they also share similar genetic composition and environmental factors.<sup>42,43</sup> The findings of Cordain et al<sup>37</sup> may have been bolstered if the acne-free subjects were given diets rich in high-glycemic foods with subsequent development of acne.<sup>42</sup>

Recent noteworthy advances have been made in our understanding of the complex interrelationships among hyperandrogenism, hyperinsulinemia, and acne. We summarize the highlights of these advances below. However, despite our evolving knowledge, the link between hyperinsulinemic, high-GI diets and acne pathogenesis remains tenuous. Recent studies present conflicting results.

It has been postulated that growth hormone may be involved in the pathogenesis of acne. IGF-1, a surrogate marker of growth hormone, is often used as an indicator of growth hormone secretion because it has little diurnal variation. In 1995, Aizawa and Niimura<sup>44</sup> sought to investigate the relationship between acne and IGF-1. They studied 82 postadolescent eumenorrheic women with acne and 31 age- and sex-matched control subjects and found that the IGF-1 levels were significantly greater in patients with acne. However, there was no correlation between IGF-1 and testosterone, free testosterone, dehydroepiandrosterone-sulfate, or acne severity. In a subsequent study, Aizawa and Niimura<sup>45</sup> sought to correlate basal insulin and glucose-stimulated insulin levels with androgen levels in women with acne. They investigated 30 eumenorrheic women

with acne and 13 control subjects. Serum-free testosterone, DHT, and dehydroepiandrosterone-sulfate were significantly higher in the acne group. Basal insulin levels were similar between the two groups, but upon administration of a 75-g, 2-hour oral glucose tolerance test, summed insulin levels were significantly higher in the acne group. However, there was no significant difference in the change in serum testosterone or free testosterone during the oral glucose tolerance test between the two groups. The authors concluded that there was mild insulin resistance during the oral glucose tolerance test in patients with acne, but that the postprandial hyperinsulinemia did not determine hyperandrogenemia in patients with acne. This study was limited by small sample size and lack of generalizability beyond eumenorrheic women.

A recent cross-sectional study by Kaymak et al<sup>46</sup> measured fasting glucose, insulin, IGF-1, IGFBP-3, and leptin levels in 49 Turkish university students with acne and 42 healthy control subjects. All subjects also completed a food frequency questionnaire from which investigators calculated overall GI and dietary glycemic load. No significant differences in serum glucose, insulin levels, leptin levels, overall GI, and dietary glycemic load between patients with acne and control subjects were found. The authors concluded that these variables are not involved in the pathogenesis of acne.

This study has been criticized for using a diet-assessment tool that was never validated, and for not providing it in the article, making one unable to assess the robustness of the instrument.<sup>47</sup> In addition, the timing of phlebotomy has been criticized. Fasting levels of serum markers were used, and do not represent insulin level excursions and total insulin exposure over the course of the day.<sup>47</sup> To detect mild insulin resistance, which is the kind expected in this otherwise healthy population, repeated measures of serum markers must be drawn at multiple intervals postprandially. Another drawback of the study was the failure to assign GI and glycemic load values for meat, poultry, fish, vegetables, and cheese. The authors stated that these foods are not likely to induce a significant increase in blood glucose. However, dietary fish rich in omega-3 fatty acids can improve glycemic control, whereas processed meats can impair glycemic control. In addition, vegetable cooking technique can affect glycemic load.<sup>47</sup> By focusing only on carbohydrates, the study failed to account for the impact of other foods. Interestingly, the levels of IGF-1 were significantly higher among patients with acne as compared with control subjects. Furthermore, the levels of IGFBP-3 were significantly lower among patients with acne as

compared with control subjects. These findings, although supportive of an association between free, and consequently active, IGF-1 serum levels and acne, were merely mentioned in the results and never addressed in the discussion of the article.<sup>47</sup> These values were incorrectly reported in the table (Table II) of the publication, showing a reversal of the data as they were reported in the "Results" section. Clearly, not much attention was paid to these findings. Another piece of evidence that may have been overlooked was the finding that overall GI levels of patients whose disease duration was more than 2 years were significantly higher than patients with less than 2 years of disease duration. Consequently, this purportedly "negative study" had several positive findings of potential interest. Lastly, the results of this study are not generalizable to postadolescent patients with acne, in whom dietary influence may play a greater role than is seen in hormonally sensitive adolescent patients.

The most convincing evidence to date of an association between glycemic load and acne was a recently published randomized controlled trial conducted by Smith et al,<sup>48,49</sup> demonstrating significant improvement in acne severity in 23 Australian males ages 15-25 adhering to a LGL diet. The LGL diet also resulted in significant reductions in weight, body mass index (BMI), and free androgen index as well as increased IGF-1 and improved insulin sensitivity. This preliminary study had several strengths, including its randomized controlled trial design, blinded dermatologic assessments, and multiple measures taken to ensure dietary compliance (staple foods provided, individual dietary counseling, careful food records, regular telephone interviews, urinary samples). That being said, the study did suffer from several limitations. First, the independent effects of weight loss and dietary intervention were not isolated from one another. The participants in the LGL group lost weight (and decreased their BMI), precluding the authors from solely attributing the treatment effect to a change in glycemic load. Adjusting the study end points for the change in BMI altered several of the study outcomes. Specifically, the associations between LGL diet and total lesion counts as well as LGL diet and insulin resistance both lost statistical significance after adjusting for BMI. Other dietary factors such as fat intake and dietary fiber intake might also have differed between the two groups, thereby accounting for part of the treatment effect. Lastly, the results of this study cannot be generalized to female adolescents who undergo different and potentially cyclical hormonal changes that may themselves interact with the effect of diet on acne.

Most recently in 2008, Smith et al<sup>50</sup> designed a pilot, prospective cohort study in which 12 male patients with acne were admitted to a research facility and consumed controlled feedings of either LGL or high glycemic load (HGL) diets for 7 days. The researchers found that subjects adhering to the LGL diet demonstrated improvements in insulin sensitivity when compared with the HGL group. Furthermore, the HGL diet significantly increased androgen bioavailability, whereas increases in IGF-1 in the LGL group suggested a reduction in IGF-1 activity. The authors concluded that increased glycemic load may result in increased activity of sex hormones and IGF-1, thereby contributing to acne development. Although this study is notable for its precise control in the composition of foods provided and its careful recording of dietary intakes, this study does have a few limitations. Sample size was small and subjects were not randomized to treatment groups, thus introducing the potential for selection bias. Similar to the previous study described above, results cannot be generalized to female patients or anyone outside of the 15- to 20-year-old age range.

In addition to its effect on hormonal cascades, diet has also been implicated in the pathogenesis of acne by altering sebum composition. In 2008, Smith et al<sup>51</sup> designed a randomized controlled trial in which 31 male patients with acne were assigned to either a LGL diet or a control diet for 12 weeks. A blinded investigator assessed subjects' acne occurrence and severity. Skin surface lipids were collected via lipid-absorbent strips applied to the forehead. Sebum outflow and fatty acid composition of skin surface triglycerides were calculated. Compared with the control group, the members of the LGL group had an increased ratio of skin surface saturated fatty acids to monounsaturated fatty acids. This ratio was negatively associated with number of acne lesions. Increased follicular sebum outflow was also correlated with increased proportion of sebum monounsaturated fatty acids. These findings suggest a possible role of desaturase enzyme in sebaceous lipogenesis and the severity of acne. The results of this study may have been confounded by the fact that the LGL dietary group lost weight, and that the effects of dietary consumption could not be isolated from the effects of weight loss. Another limitation of the study is that the results cannot be generalized to female patients or patients outside of the 15- to 25-year-old age range.

Some of the most compelling evidence suggesting an association between diet and acne comes from patients with polycystic ovarian syndrome, a condition with a constellation of features including insulin resistance, hyperinsulinemia, hyperandrogenism, and acne.<sup>52</sup> Studies have demonstrated that acne

improves when these patients are treated with medications that improve insulin metabolism such as metformin, tolbutamide, pioglitazone, and acarbose.<sup>53,54</sup> These patients did not receive acne therapy as part of the study protocols. Of note, improvement in acne was not a primary end point for any of these trials. A low-carbohydrate ketogenic diet has been shown to improve androgen profiles in patients with polycystic ovarian syndrome.<sup>55</sup>

The most recent scientific contribution supporting an association between carbohydrate intake and acne severity comes from a World Wide Web-based survey used to assess a possible role for the South Beach diet in the treatment of acne.<sup>56</sup> The South Beach diet is considered a low-glycemic diet, and mimics the nutritional characteristics of diets found in non-Westernized societies. It emphasizes unprocessed, fresh fruits, vegetables and lean meats, fish, and seafood. A total of 2528 self-proclaimed “active dieters” completed the online survey. Approximately 75% of these patients reported acne lesions, and 86.7% of these respondents noted improvements in their skin. Of those respondents already on treatment for their acne, 91% decreased the dose or amount of the acne treatment they were using. This study design is far from ideal, as recognized by the researchers, and thus the results must be interpreted with cautious optimism. In fact, the study suffers from at least 3 forms of bias. First, the study suffers from selection bias, in that subjects who clicked the online link to fill out the survey are most likely to represent those people who are very enthusiastic about the diet and therefore likely to visit the World Wide Web site regularly and endorse the diet in any way possible. Those who found the diet hard to follow, who found the diet ineffective, or whose acne worsened as a result of the diet would be much less likely to visit the World Wide Web site regularly, let alone voluntarily respond to a survey linked to this World Wide Web site. In addition, the study likely suffers from misclassification bias in that subjects with acne might have been classified as not having acne, whereas those without acne might have been classified as having acne. Both the diagnosis of acne and the reported improvement in acne were self-reported and not verified by a physician or objective examination. Studies that have compared self-report of acne with objective acne assessments have shown that people with acne are not able to accurately report that they have acne.<sup>35</sup> Validity of self-report is moderate at best. Furthermore, recall bias may be playing a role in this study. Subjects who are partial to the South Beach diet because of its effect on their weight or self-image are more likely to recall an improvement in their acne and attribute this

improvement to the diet. Lastly, the association between the diet and acne improvement might have been confounded by weight loss or exercise. Patients on the diet are likely to have lost weight, incorporated exercise into their weight management plan, or both. The weight loss itself, or the exercise, might have impacted on the acne more than the restriction of high-GI foods, and thus must be accounted for in future studies.

Although the current literature examining the association between carbohydrate intake and acne has used GI and/or glycemic load as a marker of glycemic impact, one must note that controversy exists regarding the use of these measurements. The GI of a particular food is defined as the area under the blood glucose time curve for 2 hours after ingestion of a fixed portion of that food containing 50 g of carbohydrate. The GI of a standard (either glucose or white bread) is taken as 100. The GI thus is intended to reflect the relative effect of different food on blood glucose. The average GI for a single food is calculated from data collected from 10 human subjects.<sup>57</sup> Glycemic load is calculated for a given quantity of food by multiplying by the carbohydrate in the portion of the food.<sup>57</sup> The GI of a single food may vary from one source to another unless corrected for the difference in choice of the reference food (glucose vs white bread). It has also been argued that neither the GI nor the glycemic load are able to accurately predict the glycemic responses elicited by mixed meals.<sup>58,59</sup> The question remains controversial, as other researchers have been able to use the carbohydrate content and GI to predict about 90% of the variation in the mean glycemic response.<sup>60</sup> These authors also claim the effects of protein and fat on the glycemic response were negligible although this seems unlikely in general because both are known to slow absorption of food which is a contributor to the GI. Furthermore, data by Gannon et al,<sup>61</sup> for example, although not specifically discussing GI, have shown that the presence of fat does affect blood glucose in healthy people but, significantly, not in people with diabetes.

#### **MORE MODERN STUDIES REVISIT THE LINK BETWEEN ACNE AND DIET: MISCELLANEOUS FACTORS THAT MIGHT POTENTIALLY INFLUENCE ACNE SEVERITY**

##### **Omega-3 fatty acids and acne**

The relative intake of omega-6 to omega-3 polyunsaturated fatty acids is an important dietary modulator of inflammation.<sup>15,62</sup> The typical Western diet contains a higher ratio of omega-6 to omega-3 fatty acids compared with the hunter-gatherer diet that is

rich in fish, wild game, and wild plants.<sup>63</sup> As described earlier, Cordain et al<sup>37</sup> suggested that the absence of acne in the Kitavan and Aché may have directly been related to their low-glycemic diets. However, it has also been postulated that the higher content of omega-3 fatty acids in the diets of these populations may have also played a role.<sup>63</sup> Increased relative consumption of omega-3 polyunsaturated fatty acids may suppress inflammatory cytokine production, thereby exerting a therapeutic effect on acne.<sup>15</sup> Because omega-3 fatty acids inhibit synthesis of the inflammatory molecule leukotriene B<sub>4</sub>, and blockage of leukotriene B<sub>4</sub> leads to reduced inflammatory acne lesions,<sup>64</sup> it has been postulated that increased consumption of omega-3 polyunsaturated fatty acids may reduce inflammatory acne.<sup>15</sup> Omega-3 fatty acids have also been shown to decrease IGF-1,<sup>65</sup> which, as described earlier, has been implicated in the exacerbation of acne.

Very few human studies examining the effect of omega-3 fatty acid ingestion on acne have been conducted. One epidemiologic study in 1961 found that adolescents consuming large amounts of fish and seafood, rich sources of omega-3 fatty acids, appeared to be less likely to manifest acneiform lesions on examination.<sup>66</sup> A very limited case series of 5 patients with acne using an omega-3-based dietary supplement [containing eicosapentaenoic acid from fish oil, (–)epigallocatechin-3-gallate, zinc gluconate, selenium, and chromium] suggested possible improvement in inflammatory papules and global aspects of well-being.<sup>67</sup> Further research is clearly needed to establish the clinical significance of omega-3 fatty acids in treatment of acne.

### Antioxidants and acne

Reactive oxygen species produced by neutrophils are involved in the inflammatory progression of acne.<sup>68</sup> Reactive oxygen species are normally removed by cellular antioxidants such as glucose-6-phosphate dehydrogenase and catalase, both of which are present in lower quantities in patients with acne.<sup>69</sup> Malondialdehyde, a marker of lipid peroxidation and oxidative damage, has been reported to be higher in patients with acne compared with control subjects.<sup>69,70</sup> It has been suggested that oxidative stress may be implicated in the origin of acne and that drugs with antioxidant effects (or antioxidant supplements) may be valuable adjuvants in acne treatment.<sup>69,70</sup>

El-Akawi et al<sup>71</sup> recently conducted a cross-sectional study comparing blood levels of lipid-soluble antioxidants (vitamins A and E) in 100 patients with acne to levels in 100 healthy control subjects without acne. They found that subjects with

acne had significantly lower plasma concentrations of these antioxidants as compared with the control subjects. Low levels of blood selenium have also been documented in patients with acne.<sup>72</sup> Because the selenium-dependent glutathione peroxidase enzyme activity is low in patients with acne, it is possible that selenium supplementation may be of value in acne. One study examined the effect of selenium and vitamin E supplementation for 12 weeks in acne. The study was not blinded and included no control group, so although the combination led to improvements in acne, the data are of limited value.<sup>73</sup> A catechin found in green tea, (–)epigallocatechin-3-gallate, has been heralded for its antioxidant properties. Topical application of (–)epigallocatechin-3-gallate on male hamster forehead skin has been shown to inhibit sebum production.<sup>74</sup> Nobiletin, a flavonoid with antioxidant properties, is found in the juice of *Citrus depressa* Hayata.<sup>75</sup> In hamster auricles, nobiletin has been shown to inhibit lipogenesis and cell proliferation in sebaceous glands and facilitate the excretion of sebum from mature sebocytes.<sup>75</sup> In vitro, the flavonoids kaempferol and quercetin (found in flowers of *Impatiens balsamina*, a plant used in traditional Eastern medicine) have been shown to possess antibacterial activities against *Propionibacterium acnes*, a major causative agent in acne.<sup>76</sup> Finally, resveratrol, a phytoalexin found in the skins of red grapes, red wine, peanuts, mulberries, spruce, and eucalyptus, may be another promising antioxidant therapy for acne. In vitro, resveratrol has been shown to be bacteriocidal against *P acnes*.<sup>77</sup> There is growing basic science literature supporting the role of antioxidants in acne therapy. However, the clinical significance of naturally occurring antioxidants in plant foods as treatment for acne remains yet to be established.

### Zinc and acne

Zinc is a metallic chemical element that is essential for the proper development and functioning of human skin.<sup>78</sup> Approximately 6% of the body's supply of zinc is located in the skin.<sup>79</sup> Zinc sulfate was the first chemical form of zinc available, however, in the 1980s it was replaced by zinc gluconate because of its superior bioavailability. The increased bioavailability of zinc gluconate enabled a decrease in the dose of oral zinc administered, thereby improving gastrointestinal tolerability.

In the 1970s, Michaelsson<sup>80</sup> and Fitzherbert<sup>81</sup> were the first to provide evidence that acne improved with oral zinc supplementation in zinc-deficient patients. Patients with acne were reported to have low levels of serum zinc.<sup>82,83</sup> Subsequently,

randomized double-blind placebo-controlled trials<sup>84-89</sup> and a randomized double-blind trial of zinc versus minocycline<sup>90</sup> showed that oral zinc was effective in the treatment of severe and inflammatory acne, more so than mild or moderate acne.<sup>91,92</sup> These trials did not control for other dietary factors. Zinc is bacteriostatic against *P acnes*, inhibits chemotaxis, and may decrease production of the inflammatory cytokine tumor necrosis factor- $\alpha$ .<sup>93</sup> However, the oral doses of zinc used in the majority of these studies (200 mg/d of zinc gluconate, 400 or 600 mg/d of zinc sulfate) were associated with nausea, vomiting, and diarrhea.<sup>85,86,89,92,94</sup> Gastrointestinal side effects can be somewhat reduced by consuming zinc directly after meals. Because zinc decreases the absorption of copper, 1 to 2 mg of copper supplementation may be recommended in patients on chronic zinc therapy to prevent copper deficiency. Oral zinc salt supplementation has been shown to be equal or less effective than oral tetracyclines.<sup>80,90,95</sup> One study showed that 8 weeks of 411 mg of daily oral zinc sulfate therapy had no effect on male patients with moderate acne, despite documented systemic absorption.<sup>91</sup> However, this study included a placebo washout period in which there was a significant improvement in acne, thereby leaving little room for further improvement with zinc. Most of the studies examining the effect of oral zinc on acne severity were limited by small sample sizes. The study of Dreno et al<sup>90</sup> in 2001 was the only study to include more than 60 subjects. Given the evidence to date, the use of oral zinc as treatment for acne is limited by poor patient compliance secondary to gastrointestinal side effects and by limited efficacy compared with oral antibiotics. Given the increasing worldwide prevalence of antibiotic-resistant *P acnes*, a modern trial designed to compare oral zinc therapy with oral antibiotics might show very different results. Future research should be directed at investigating the efficacy and side effects of lower doses of oral zinc.

### Vitamin A and acne

Dietary vitamin A is obtained either from preformed vitamin A or from provitamin A carotenoids. Preformed vitamin A is efficiently absorbed and used by human beings, and is largely derived from multivitamins, fish liver oil, and fortified foods such as milk, butter, margarine, and breakfast cereals. In contrast, provitamin A carotenoids are derived from plant sources and are absorbed much less efficiently. Consequently, absorption and hepatic storage of preformed vitamin A occur very efficiently until a pathologic condition develops, whereas toxicity from provitamin A sources is largely impossible.<sup>96</sup>

**Table III.** Cited recommendations regarding calcium<sup>109</sup> and vitamin D supplementation<sup>105,109</sup>

Age, y	Calcium intake, mg/d (mmol/d)	Vitamin D intake, $\mu$ g (IU)
9-18	1300 (32.5)	10 (400)
19-50	1000 (25)	5 (200)
51-70	1200 (30)	10 (400)
$\geq 71$	1200 (30)	15 (600)

Several experts are recommending significantly higher doses of vitamin D, with recommendations reaching as high as 2000 IU per day for an adult.

Most dermatologists are reluctant to recommend oral vitamin A supplements for acne because of the fear of inducing hypervitaminosis A. Hypervitaminosis A refers to the effects of excessive vitamin A intake, and includes hepatotoxicity, teratogenicity, reduced bone mineral density that may result in osteoporosis, alopecia, xerosis, and pseudotumor cerebri.<sup>97</sup>

Kligman et al,<sup>98</sup> in 1981, reported that oral vitamin A (retinol) is effective in acne treatment when used in high doses (300,000 U daily for women, 400,000-500,000 U daily for men). These authors declared that the danger of hypervitaminosis A in this dosage range has been exaggerated, as they observed minor adverse events, mostly limited to xerosis and cheilitis. However, supplementation was only given for 4 months in this study, and safety concerns (particularly liver toxicity) are likely to arise if such high doses of oral vitamin A are sustained for a longer period of time.

### Dietary fiber and acne

No clinical studies have specifically examined the role of dietary fiber in acne treatment. Anecdotally, Kaufman<sup>99</sup> has reported significant improvement of acne in patients consuming 30 g of high-fiber breakfast cereal (13 g of fiber/serving) every day. As described earlier, Smith et al<sup>48</sup> reported improved acne in patients on a LGL diet. It has been suggested that the results of this study may have been confounded by the higher daily consumption of dietary fiber in patients on the LGL diet and that the increased fiber content may have actually been the therapeutic part of the diet.<sup>100</sup> Further studies should examine the potential value of a high-fiber diet in treating acne.

### Iodine and acne

Iodine has long been implicated as a cause of acne vulgaris, however, no literature to date supports iodine as a culprit in comedonal acne.<sup>101</sup> Acne resulting from iodine consumption typically presents as an abrupt, monomorphic eruption of predominantly pustules. Kelp, a form of seaweed rich in

**Table IV.** Side effects of excess dietary supplementation

Dietary supplement	Side effects of excess consumption
Omega-3 fatty acids	Fishy aftertaste, abdominal pain, diarrhea, and easy bruising/bleeding
Antioxidants	
Green tea (contains EGCG)	Insomnia, increased urination, and anxiety caused by caffeine in green tea
Nobiletin, kaempferol, quercetin, resveratrol	Further research needs to be done to assess side effects
Vitamin C	Diarrhea and nausea
Vitamin E	Increased risk of bleeding, nausea, and diarrhea
Zinc	Nausea, vomiting, abdominal cramps, and diarrhea
Vitamin A	Nausea, vomiting, headaches, dizziness, fatigue, blurred vision, bone pain and swelling, osteoporosis, itching, liver toxicity, hair loss, dry skin, increased intracranial pressure, and birth defects
Dietary fiber	Flatulence, bloating, and abdominal cramps

EGCG, (–)Epigallocatechin-3-gallate.

iodine, and other systemic drugs containing iodine can cause this characteristic acneiform eruption<sup>102,103</sup> In 1961, the relationship between acne and iodine was first refuted when it was found that adolescents who consumed a diet high in seafood and fish, both rich in iodine, had lower rates of acne.<sup>66</sup> However, this study was confounded by the patients' high dietary content of omega-3 fatty acids, which, as discussed earlier, may be therapeutic in acne. More recently, it has been hypothesized that the association between milk and acne reported by Adebamowo et al<sup>17</sup> may be a result of the iodine content of milk,<sup>33</sup> which can vary with time of year, location, fortification of animal feed, and use of iodophor-sanitizing solutions.<sup>104</sup>

## CONCLUSIONS

In summary, it is evident that dermatologists can no longer dismiss the association between diet and acne. Although the link between dairy and acne is less convincing than that between a HGL diet and acne, both deserve consideration during any dietary counseling efforts. Adebamowo et al<sup>17,21,34</sup> have provided consistent data in support of an epidemiologically weak association between dairy and acne. Whether this is caused by the hormones in milk products or increased activity of IGF-1 remains to be determined. Given the level of evidence available, it is appropriate for physicians to counsel their patients that dairy products may incrementally aggravate their acne. Given the benefits of calcium, especially in a growing adolescent population, dermatologists should be prepared to advise those patients who choose to avoid dairy products to supplement their diet with appropriate levels of calcium and vitamin D (Table III). There is controversy surrounding whether the recommendations for vitamin D intake should be revised. Recently, the recommendation for vitamin D intake in

the pediatric population was doubled, and similar changes in the adult populations may follow.<sup>105</sup>

The association between a HGL diet and acne severity appears to be more substantiated, especially given the recent investigations by Smith et al.<sup>48-51</sup> Before any strong recommendations can be made regarding carbohydrate restriction among patients with acne, these results must be substantiated by different research groups, preferably using subjects from the United States spanning a larger age range and both sexes. A large randomized clinical trial with subsequent subgroup analyses to determine which baseline characteristics predict a positive response to such a diet would be ideal. One particular subgroup that deserves particular attention is women with polycystic ovarian syndrome, in whom it makes the most theoretical sense that such a diet would impact on acne. Until these further studies are executed, it is appropriate for dermatologists to recommend a LGL diet to patients with acne as an adjunct to their existing acne therapy. Based on the authors' personal experiences, dietary counseling is most challenging among patients from lower socioeconomic classes and among patients who, based on cultural background, incorporate large amounts of carbohydrates as staples in their diets (eg, Caribbean, Korean, Japanese, and Indian patients).

The roles of omega-3 fatty acids, antioxidants, zinc, vitamin A, and dietary fiber in acne vulgaris remain to be elucidated. Given the level of evidence available, the authors currently advise their patients to supplement their diets based on personal preferences and experiences, remaining vigilant for signs of intolerance or toxicity. Please refer to Table IV for a list of side effects that should serve as warnings to limit dietary supplementation.

As has always been the case, physicians will benefit by listening to their patients. If a particular

patient notes an association between a certain dietary factor and acne severity, it is most sensible to support that patient's dietary supplementation/restriction, encouraging the patient to keep a food diary to test his or her hypothesis. In light of the last decade of research investigating the relationship between diet and acne, it is no longer dermatologic dogma to state that any association between diet and acne is mere myth. This is a truly exciting avenue of research, and one that is unfortunately not funded by pharmaceutical companies. Hopefully we do not let this financial constraint deter us from pursuing this line of research with vigor and enthusiasm.

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