

Diet and Acne Revisited

THE ARTICLE by Cordain et al¹ in this issue of the ARCHIVES represents an interesting departure for a contemporary, peer-reviewed medical journal. While the present-day emphasis is on controlled, double-blinded clinical studies that pass the muster for evidence-based medicine, the report by Cordain et al is observational, and the only control is the dietary limitations characteristic of 2 isolated nonwesternized populations.

These authors suggest that the absence of acne in more than 1300 subjects in 2 nonwesternized societies—the Kitavan Islanders of Papua New Guinea and Aché hunter-gatherers of Paraguay—is attributable to their diets, which have a substantially lower glycemic index than a Western diet. In addition, these people are more physically active than Westerners. They do not demonstrate insulin resistance, nor do they have obesity, hypertension, diabetes, or heart disease. Their genetic background is similar to other Pacific Islanders and South American Indians, respectively, yet their incidence of acne is lower than that of members of these same groups who have incorporated elements of a Western diet.

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Isolated observations and case reports suggest that acne can develop in groups not generally susceptible to this disorder when a highly glycemic diet is adopted, which can induce acute or chronic hyperinsulinemia, as in the case of Eskimos who adopted a Western diet.² One of us (J.S.S.) has also heard many young Irish women report that they had no acne until they immigrated to the New England area from rural Ireland. However, no systematic studies are available to fully support or refute these observations. Of course, the study by Cordain et al¹ would have benefited from the opportunity to provide the subjects with a diet containing highly glycemic foods to determine if acne occurred, but this was not possible.

The relationship of acne to foods is certainly not new. The “big three” US textbooks of dermatology³⁻⁵ popular in the early 1950s when one of us (J.S.S.) was in training all contained elaborate prose regarding specific foods to avoid. The admonition to avoid chocolate, fats, sweets, and carbonated beverages was commonly given to patients as part of acne therapy. But all of this dietary advice was removed from standard texts, and it has been many years since restriction of specific foods has been recommended in managing acne. Nonetheless, few of us feel compelled to argue strongly with the occasional patient who insists that his or her acne is exacerbated by a certain food item. It should be noted, however, that it was reported in an article published only last year⁶ that 30% of medical students surveyed in Australia believed that acne was influenced by diet.

Cordain et al¹ suggest that diet-induced hyperinsulinemia elicits endocrine responses that may affect the development of acne through mediators such as androgens, insulinlike growth factor (IGF) 1, IGF binding protein 3, and retinoid signaling pathways. The role of diet in endocrine activity is supported by the observation that improvements in nutrition have been linked to an earlier onset of sexual maturation and the development of acne in young girls and boys. Numerous studies have shown that improvements in general nutrition in girls have led to an earlier onset of menses and that menses is delayed in girls with low body fat such as athletes and ballet dancers.⁷ In 1970, the mean age of onset of menarche in the United States was 12 years compared with age 16 years for girls in 1835.⁸ Of interest is the observation that the mean age of onset of menarche in the Kitavan population is 16 years, which is significantly older than girls in westernized societies. In a 5-year longitudinal cohort study of 439 black girls and 432 white girls in Cincinnati, Ohio, Lucky et al⁹ demonstrated that those with severe comedonal acne had a significantly earlier age of onset of menarche and higher serum levels of dehydroepiandrosterone than girls with mild comedonal acne. This study demonstrated that the early development of comedonal acne might be one of the best predictors of later, more severe disease. In a similar 5-year longitudinal study of 219 black and 249 white early adolescent boys in Cincinnati, black boys had higher pubertal maturation scores than white boys of the same age.¹⁰ The prevalence and severity of acne correlated well with advancing pubertal maturation. Is the late onset of menarche in Kitavan girls “protective” against the development of acne or severe acne? Although Cordain et al do not present data regarding the age of sexual maturation of the Kitavan or Aché boys, is it also possible that their relative lack of acne might relate to a later age of pubertal maturation and sebaceous gland exposure to higher circulating levels of androgen?

If acne results from hyperinsulinemia, as proposed by Cordain et al,¹ one would expect that obese individuals, who are relatively chronically insulin resistant, would have a higher prevalence of acne. Bourne and Jacobs¹¹ evaluated 2720 military recruits for obesity and the presence of acne and noted an association between the 2 in the older recruits (ages 20-40 years) but not in those in the age range of 15 to 19 years. This observation suggests that the presence of acne in a younger population may be associated with factors other than obesity or insulin resistance. In fact, serum levels of IGF-1 are highest during periods of the adolescent growth spurt and taper off in the 20s, which coincides with the pattern in the peak incidence of acne.¹² Insulinlike growth factor 1 functions similarly to insulin in that it can promote the growth of keratinocytes and sebaceous glands. It is possible that the effects of the hyperinsulinemia on acne in obese adolescents may be overshadowed by the effects of high

levels of circulating IGF-1. As pointed out by Cordain et al, acne has been associated with elevated serum levels of IGF-1 in adult women with acne.¹³ All adolescents, including the Kitavan and Aché, would experience increases in IGF-1 during adolescence, so increases in IGF-1 alone cannot explain the presence of acne.

Within the past few years, tremendous advances have been made in our understanding of the molecular mechanisms of obesity, insulin resistance, diabetes, and hyperandrogenism. For example, the association of hyperandrogenism and acne in women with conditions such as polycystic ovarian syndrome (PCOS) has been clearly established. In women with PCOS, insulin resistance can lead to hyperandrogenism, which then can lead to the exacerbation of acne. The treatment of PCOS now includes drugs such as thiazolidinediones and metformin, which are aimed at increasing insulin sensitivity. The reduction in serum insulin concentration has been linked to a reduction in the level of serum androgens and improvement in fertility.¹⁴ Whether this reduction in serum insulin and androgen levels equates with an improvement in acne remains to be determined.

Interestingly, not all women with PCOS are obese. Hyperandrogenism, insulin resistance, and acne still occur in lean women with this disorder. If hyperinsulinemia rather than hyperandrogenism exacerbated acne, we would expect to see much more acne in obese men and women with diabetes, hyperinsulinemia, and insulin resistance. This does not appear to be the case. On the other hand, type 2 diabetes is generally a disease of adults, who have lower serum levels of IGF-1 and growth hormone than adolescents. Perhaps the increasing levels of growth hormone, IGF-1, and androgens in the adolescent sets the stage for susceptibility to diet-induced hyperinsulinemia as a trigger for the development of acne.

Although Cordain et al¹ make a strong argument for the role of diet in acne, we believe that it is difficult to dissociate environmental factors such as diet from genetic factors in their study. The Aché and Kitavan people live in closely knit communities, and therefore genetic factors may play a role in the relative lack of acne in these populations. Several studies point to an association of genetic factors with acne, including studies that demonstrate variations in the prevalence of acne among ethnic groups and the high degree of concordance of acne in twins.¹⁵⁻¹⁹

In fact, numerous studies have failed to demonstrate significant differences in sebum composition between subjects with and without acne, suggesting that overall sebum production and not sebum composition is more important in the development of acne. During periods of starvation, when total caloric consumption is greatly reduced, sebum production is decreased by about 40%,^{20,21} which could certainly improve acne. However, this reduction occurred with extreme caloric restriction (<100 calories/d [<418 J/d]), a circumstance that is not practical to apply as a therapy, to say the least. In each of these studies, changes in the quantity and quality of sebum were reversed after a normal diet was resumed. Biochemical studies clearly demonstrate that the sebaceous gland can make lipids (cholesterol, squalene, triglycerides, wax esters, and cholesterol esters) from a variety of substrates (including acetate, glucose, and fatty acids) that serve to donate 2 car-

bon fragments.^{22,23} The starvation studies indicate that a dietary source of substrates is needed to produce sebaceous lipids. The type of food from which substrates are derived may not be important in overall sebum production.

In summary, as proposed by Cordain et al,¹ it remains possible that adolescents in westernized societies may be repeatedly acutely hyperinsulinemic due to their highly glycemic diet. Hyperinsulinemia in turn may initiate an endocrine cascade that affects the sebaceous gland and follicular keratinization and involves IGF, IGF binding protein 3, androgens, and retinoid signaling pathways. Whether adherence to a diet with a low glycemic load can alter acne in other populations is unknown.

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