COMMENTS AND OPINIONS

Fill the Mind—and Exercise It, Too!

I read with pleasure Dr. Roncinito's essay titled "Going to see Jack" in the "Art and the Calling" section of the November 2003 issue of the Archives. I return to Samuel Johnson and to the unique turn of mind of that polymath in a poignant reminder of our own intellectual obligations to our art and to our calling. In seeking to capture the distinctive masculinity of Johnson in his own work, Roncinito quotes him as writing that after a "hard journey" in the Scottish highlands... I should have been sorry to have missed any of the inconveniences, to have had more light, or less, for their cooperation crowded the scene, and filled the mind." Roncinito then continued, in his own words, as follows: "Filled the mind—that surely is the key to our professional well-being.

After having persisted the rest of the essay, I am prompted to suggest that as important as it is that the mind be filled, it is just as essential that the mind be exercised effectively by distill of topical, critical, aesthetic thoughts and that brings me to 3 interments made in different articles in the same issue but not only are cliches but also, in my opinion, contain ideas that should be passed. (1) "Acinic keratosis (AK) are paracancrotic epidermal lesions found most frequently on areas of the skin exposed to the sun. (2) "Basal cell carcinoma (BCC) is the most common skin cancer in whites, with a steadily increasing incidence. (3) The unusual incidence of malignant melanoma per 100,000 individuals almost tripled among American men, from 6.7 in 1973 to 19.1 in 1997, and more than doubled among American women, from 7.5 to 13.8 for the same period. (4) I believe that all evidence leads to the conclusion that acinic keratosis is not a paraquamous basal cell carcinoma, (5) that the most common acinic skin lesions, that has quamous cell carcinoma (of which acinic keratosis is a type), not basal, basal cell carcinoma, is the most common cancer of the skin, and that there is no epidemic of melanoma. (5) In sum, as wonderful as it is to fill the mind, it is equally as marvellous to see it as a critical manner.

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The Unwelcome Return of the Acne Diet

Commenting on the subject of reminiscence, Samuel Johnson (1709-1784) called it a triumph of hope over experience. His wisdom might well apply to dermatology's renewed interest in a possible distinct acne connection as proposed in the article "Acne Vulgaris. A Disease of Western Civilization." This observation presents an ambivalence comparison of processed snack foods with positive dietary staples implying that all westerners consume higher glycemic load than do natives of nonindustrialized countries. In fact, compared with the high-fat and dairy content of the US diet, primitive diets often derive a greater share of total calories from starchy foods like bread, rice, corn products, potatoes, and refined flour. Thus, American jobs not inclined toward sweets and soft drinks probably consume relatively low glycemic loads yet still are acne prone. The authors' theories are speculative at best. Their suggestion that diet-induced hyperinsulinemia and elevated levels of free malnolin growth factor 3 cause acne via overproduction of ovarian and testicular hormones is unlikely for several reasons. First, acne prevalence among premenarchial girls is correlated with adrenal rather than ovarian androgens, and further, hormone levels are normal in most patients with acne. Also, there is a distinct demographic divide between populations with acne vulgaris, primarily a teenage disorder, and those showing insulin resistance, mainly overweight adults. Finally, acne was ubiquitous in American adolescents 3 decades ago, prior to the proliferation of soda and candy machines in secondary schools, when the teenage obesity rate was only the third of today's 1.4%.

The suggestion that diet-related reduction of insulin-like growth factor binding protein 3 causes acne by interfering with insulin metabolism might be intriguing, except that vitamin A deficiency severe enough to cause follicular hyperkeratosis is associated with severe acne, not acne. In an isolated subspecies, attributing disease protection to a single variable like dietary glycemic index is...
Diet and Acne Redux

The science of nutrition has produced dramatic findings over the past two decades. Of particular note is the expansion of knowledge about essential fatty acids during the 1980s. Also, profound changes in the concepts of daily nutritional requirements find the United States replacing "recommended daily allowances" with "dietary reference intakes." This reflects the consideration of optimal nutrient levels rather than minimum daily requirements. The vitamin paradigm changed forever when neural tube defects declined radically with folic acid supplementation.

No longer do we think only of preventing nutritional deficiencies. Now we are learning to provide optimal nutrient intake for optimal function.

Cardiologists have embraced this concept and now prescribe the vitamin B6, vitamin B12, and folate to bring down elevated homocysteine levels in patients at risk for stroke and myocardial infarction. Although causality has not been proved, study findings are highly suggestive, and supplementation curtails few risks. The American Heart Association also acknowledges the benefit of daily fish oil supplementation for some patients.

However, few physicians in other fields seem to take advantage of recent discoveries in nutrition and apply them clinically.

Dermatologists have been particularly tied to older nutrition dogmas with regard to acne and diet. The article by Cordain et al in a recent issue of ARCHIVES should serve to awaken us to the relevance of nutrition to skin disease and steer us to review the dogma. The major text books of dermatology tend to view diet as irrelevant to the treatment of acne. The primary references to which the text refers are both more than 20 years old.

In 1971, Anderson observed 27 college students on a "typical high-carbohydrate down diet." The students believed that specific foods caused inflammatory flares within 3 days of ingestion. They received the culprit foods on a daily basis and remained daily for facial mapping of lesions. None flared. While the uniformity of response was impressive, the study had a few glaring flaws. The sample size was fairly limited. The study was neither controlled nor blinded. The article was not peer reviewed by dermatologists (published in the American Family Physician). Most importantly, given the effects of chronically elevated insulin posited by Cordain et al., the baseline diet may have obscured the findings.

In 1969, Fulton et al explored the effect of chocolate on acne by using "pseudo-chocolate" bars made with 28% partially hydrogenated vegetable oil as the control. With our 2002 lens, we can see that the high proportion of trans fats in the control bars limits the usefulness of the study. Trans fats compete with essential fatty acids in the production of prostaglandins and appear to significantly contribute to inflammation.

In the nutrition literature, evidence supporting dietary effects on health continues to mount, and dermatology is no exception. Many of our patients' skin conditions are affected by what they eat. It may be time for us to open our minds and our nutrition textbooks.

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References:
excess of proinflammatory omega-6 and trans fatty acids, and a reduced intake of dietary antioxidant vitamins. The current ratio of omega-6 to omega-3 fatty acids in the western diet reaches 20:1, while through evolution and in a traditional hunter-gatherer diet it is closer to 1:1. Fish, wild game, and wild plants have much higher levels of omega-3 fatty acids than do refined western foods. In addition to being higher in omega-3 fatty acids, the diets consumed by the Kitavan and Aché may also include increased quantities of plant-derived antioxidants, vitamins, minerals, and phytochemicals that support antioxidant pathways. Research shows that omega-3 fatty acids can increase insulinlike growth factor binding protein 3 in animals and decrease insulinlike growth factor in healthy humans. Therefore, in support of the idea of Cordain et al.'s diet high in omega-3 fatty acids may also be involved in the prevention of the hyperkeratinization of sebaceous follicles. In addition, the involvement of proinflammatory leukotriene B4 (LTB4) in the pathogenesis of acne has recently been described; administration of a novel LTB4 blocker led to a 70% reduction in inflammatory acne lesions, improvements that correlated with a reduction in proinflammatory lipid levels. The anti-inflammatory properties of omega-3 fatty acids, including LTB4 inhibition, are well known. Arachidonic acid, the major dietary omega-6 fatty acid, is a precursor to the manufacture of LTB4, indicating that dietary choices may play a role in inflammatory acne lesions. It is possible that dietary omega-3 fatty acids could have a synergistic effect on innate potential benefit of adhering to a diet with a low glyceric level. 5GSH levels are also required. In particular, a more detailed dietary analysis of the Kitavan and Aché may help determine if additional relevant differences occur between the Kitavian and that consumed by non-westernized populations.

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In his letter, Dr. Logan suggests that a lower dietary omega-6 to omega-3 ratio, and related dietary and health habits, may play a synergistic role along with a lower glycerin load in preventing the development of acne via reductions of proinflammatory eicosanoids. This hypothesis is certainly reasonable given recent evidence showing that a LTB4 blocker led to a 70% reduction in inflammatory acne lesions after 3 months. We have previously reported that the Kitavans indeed maintain a significantly lower dietary omega-6:omega-3 ratio than do western populations and that this lower dietary omega-6:omega-3 ratio is characteristic of virtually all hunter-gatherer diets. Another feature that distinguishes Kitavan and Aché diets from western diets is the absence of milk, which exhibits a low glyceric index but paradoxically is highly insulinotropic. As with high-glyceric-load carbohydrates, dietary interventions will be required to assess the effectiveness of any nutritional treatment on the development of acne.

In her letter, Dr. Trelolour implies that "the emperors wear no clothes" by pointing out to the dermatology community that the nearly universal assumption that diet and acne are unrelated is based largely on 2 marginal and poorly designed studies that are more than 30 years old. This conclusion is not unique, a previous report summarized, "There are few, if any, well-controlled studies on the effects of various dietary factors on acne. Although the single article by Fulton et al. has been often cited as the definitive work associating diet and acne, serious design flaws in the study were identified more than 25 years ago showing that the fat and sugar content of the placebo had not differ significantly from chocolate. If high-glyceric-load carbohydrates represent the environmental trigger for the development of acne in genetically susceptible individuals, then the double-blind study by Fulton et al. would not have been able to detect a treatment effect because the glyceric load of the placebo and treatment were nearly identical." Many early 20th-century observations by dermatologists and physicians have linked sugars and refined cereals or acne. Unfortunately, at this time, these observations lacked objectivity because mechanistic understanding of the endocrine and cytokine basis underlying the development of acne was in its infancy and because well-controlled dietary interventions were rarely or never performed. Regrettably, we still cannot confirm or deny these early observations because well-controlled dietary interventions have yet to be conducted. In the 21st century, we now have the tools and knowledge to adequately test the diet-acne hypothesis—i.e., high-glyceric-load carbohydrates, insulinoceptive dairy products, trans fatty acids, a high dietary omega-6:omega-3 ratio, or all of the above.

In science, when believable facts are consistent with prevailing theory, the facts are not necessarily drawn out or ignored. Frequently, new facts make prevailing theory untenable. Our report demonstrates that an inconsistancy may exist between the observable facts (the truth absence of acne in non-westernized populations) and the prevailing theory (that diet and acne are unrelated). This information should not be viewed as an "anomalous return of the acne diet," but rather shall provide a theoretical construct for critically reexamining the diet-acne hypothesis. As Dr. Trelolour has pointed out, the current foundation for rejecting the diet-acne hypothesis is virtually nonexistent and relies almost entirely on two 20-year-old, poorly controlled studies. No further letter to the "editor" will ultimately resolve this issue. The currency of science is good data generated from well-controlled experi...
ments. Until this information becomes available, it is premature to either reject or accept the diet-acne hypothesis.

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VIGNETTES

Histologic Resolution of Melanoma in Situ (Lentigo Maligna) With 5% Imiquimod Cream

Lentigo maligna (LM) is an in situ melanoma that occurs on the face and other sun-exposed areas. Identification may histologically extend beyond the clinical borders of the lesion, therefore, obtaining clear surgical margins is difficult.

Report of a Case. A 55-year-old woman presented with an irregular, brown-to-tan, poorly differentiated, 2.3×1.9-cm patch on her right cheek that was accentuated by Wood lamp examination. The hyperpigmented area had been treated 2 years earlier with carbon dioxide laser ablation without biopsy confirmation, but the lesion had recurred and appeared to be darker and larger. A biopsy specimen showed LM (Figure 1). After a thorough discussion of treatment options, including surgical excision, cryotherapy, and radiation therapy, the patient opted for a non-surgical approach. The decision to use 5% imiquimod cream, off-label, included a detailed explanation of the risks, potential failure, and departure from the current standard of care. After the patient applied 5% imiquimod cream once or twice a day for 3 months, multiple punch biopsy specimens obtained from the tumor site showed no residual LM (Figure 2). Clinical examination and Wood lamp examination of the area also showed fading of pigmentation and no extension of the lesion.

Comment. Lentigo maligna is an in situ pattern of melanoma that occurs on sun-exposed areas, such as the face, forearms, and legs. Like other in situ melanomas, LM does not metastasize if it is completely excised. However, because the majority of LM occurs on the face, surgical excision can lead to significant disfigurement. Because LM is poorly defined clinically, excision margins are frequently violated, requiring multiple surgical procedures.

5% Imiquimod cream (Aldurav, 3M Pharmaceuticals, St Paul, MN) is a unique immunomodulator that is currently approved only for the treatment of genital warts. The medication actually modulates or up-regulates multiple cytokines to eradicate the human papillomavirus. Cytokines, such as interferon α, interleukin 12, and interferon γ, are increased in the skin at the application site, mimicking the normal host immune response to human papillomavirus eradication.7 Injectable interferon alfa has also been shown to cause resolution of actinic keratoses, squamous cell carcinoma, postauricular keloids, and superficial basal cell carcinoma.8 Currently, systemic interferon alfa is used as adjuvant therapy for metastatic melanoma.8

Figure 1. Characteristic lentiginous pattern of severely atypical melanocytes in lentigo maligna before 5% imiquimod therapy.

Figure 2. Residual normal-appearing melanocytes, with no evidence of lentigo maligna, after 3 months of 5% imiquimod therapy.