Seminars in Cutaneous Medicine and Surgery

Implications for the Role of Diet in Acne

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Within the dermatology community, a general consensus has emerged that diet is unrelated to the etiology of acne. Except for 2 poorly designed studies, now more than 30 years old, there are few objective data to support this notion. In contrast, a large body of evidence now exists showing how diet may directly or indirectly influence the following 5 proximate causes of acne: (1) increased proliferation of basal keratinocytes within the pilosebaceous duct, (2) incomplete separation of ductal corneocytes from one another via impairment of apoptosis and subsequent obstruction of the pilosebaceous duct, (3) androgen-mediated increases in sebum production, (4) colonization of the comedo by *Propionibacterium acnes*, and (5) inflammation both within and adjacent to the comedo. This article will provide a review of the currently available literature on the association between diet and acne vulgaris as well as a discussion of the physiologic principles that may underlie this association.

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During the course of the last 30 to 40 years, a general consensus has emerged within the dermatology community that diet has no role in the etiology of acne.[1-8] Comments such as "The association of diet with acne has traditionally been relegated to the category of myth"[9] are commonplace in both the past and current literature. This widely accepted perception is somewhat surprising given that a recent comprehensive review examining 250 trials of acne therapy during the past 50 years was able to identify only a single controlled study in which diet was even mentioned.[10] Moreover, 2 of the major textbooks of dermatology[1,2] promulgate the notion that diet and acne are unrelated, yet rely only on 2 primary references[11,12] that are not only more than 30 years old, but which contain key experimental design flaws.[13,14]

Because of this virtual absence of well-designed modern studies, it may be useful to critically examine the 2 dietary studies that have so strongly influenced the authors of modern textbooks of dermatology as well as to briefly examine the prior historical literature. Second, it may be insightful to examine the current literature showing how, either directly or indirectly, dietary manipulations may influence (1) the balance of steroid hormones (and hence sebum synthesis), (2) follicular keratinocyte proliferation and differentiation, and (3) inflammation. Dysregulation of these 3 fundamental physiologic mechanisms along with involvement of *Propionibacterium acnes* represents the known proximate causes of acne.[15]

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Purported Evidence against Diet as an Etiologic Agent in Acne

Given the dogma in current dermatology textbooks,[1,2] it might be assumed that there has been a long and well-established literature conclusively demonstrating that diet and acne are unrelated and that the 2 articles[11,12] most frequently cited as definitive evidence against the diet/acne hypothesis merely represent capstone studies that confirm previous observations and conclusions. In actuality, both assumptions have little factual basis.

Two reviews[7,16] of the diet/acne literature covering 80 references and spanning 66 years from 1906 to 1972 clearly demonstrate the inconclusive and conflicting nature of the historical literature. Examination of many of these early studies shows them to be rife with contradictory results and conclusions due in part to numerous limitations of study design, such as the lack of control groups, inadequate sample size, no statistical treatment of data, the lack of blinding and/or placebos, and inadequate or no baseline diet data, as well as imprecise and inconsistent measurement procedures commonly seen in early, developing technology. Furthermore, most early investigators did not have the benefit of research elucidating the endocrine mechanisms underlying acne's pathogenesis, let alone its molecular underpinnings. Accordingly, they commonly did not examine etiologic variables we now understand to be important. In summary, there is little

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substantive evidence in the historical literature that conclusively supports or refutes the role of diet in the etiology of acne.

A MEDLINE search revealed that, since 1971, no single human study has been published examining the role of diet in the etiology of acne. This paucity of recent information along with the inconclusive nature of the historical literature lends little support for the dismissal of the role of diet in the development of acne. Further, careful scrutiny of the 2 most frequently cited studies[11,12] used to refute the role of diet in the development of acne reveals serious design flaws similar to most other historical studies.

In the study conducted by Anderson in 1971,[11] 27 medical students (no age or gender reported) were asked to identify 1 of 4 culprit foods (chocolate bars, milk, peanuts, or Coca-Cola™). The subjects were then given their single culprit food (6 servings of either 39-g chocolate bars, 1137 mL of milk, 113 g of roasted [salted with iodized salt] peanuts, or 682 mL of Coca-Cola™) daily for 7 days. All facial lesions were counted and graded by size, severity, and depth once before the experiment began and then daily during the 7-day treatment period.

Unfortunately, the methods for grading or analyzing lesions were not well-described. Further, no pre- or postexperiment lesion counts were reported, nor were any of the data statistically analyzed. Consequently, the reported one-third of subjects who developed new lesions during the dietary treatment may or may not have been statistically significant. Additionally, no grouping of data by culprit food was precisely reported; accordingly, the sample size assigned to each subgroup is not known and may have lacked statistical power to detect a treatment effect, even had appropriate statistics been used. More profoundly, however, these shortcomings pale in comparison to crucial design flaws in the experiment. The subjects' baseline diet was not measured. Consequently, there is no way of knowing whether the treatment diet varied from the subjects' normal diet. Furthermore, there was no control group, nor was the experiment blinded. Accordingly, internal validity was substantially compromised in this design, making it very difficult to make meaningful interpretations of these data.

In the 1969 experiment by Fulton and co-workers,[12] 65 subjects (14 adolescent boys, 16 adolescent girls, and 35 young adult male prisoners) consumed either a 112-g bittersweet chocolate bar enriched with chocolate liquor and cocoa butter or a 112-g control bar without chocolate liquor and cocoa butter once a day for 4 weeks in a single blind crossover design with a 3-week washout period. Subject lesion counts were made at the beginning and end of the treatment and control legs of the study and organized into 3 ordinal categories: worse (lesion count increased by 30% at the end of a test period), improved (lesion count decreased by 30% at the end of a test period), and unaffected (if lesion count was less than 30% change). Fig. 1 demonstrates the results of this study. Because there were no significant differences between the chocolate and control bars in the 3 lesion count categories, the authors concluded "ingestion of high amounts of chocolate did not materially affect the course of acne vulgaris or the output or composition of sebum."

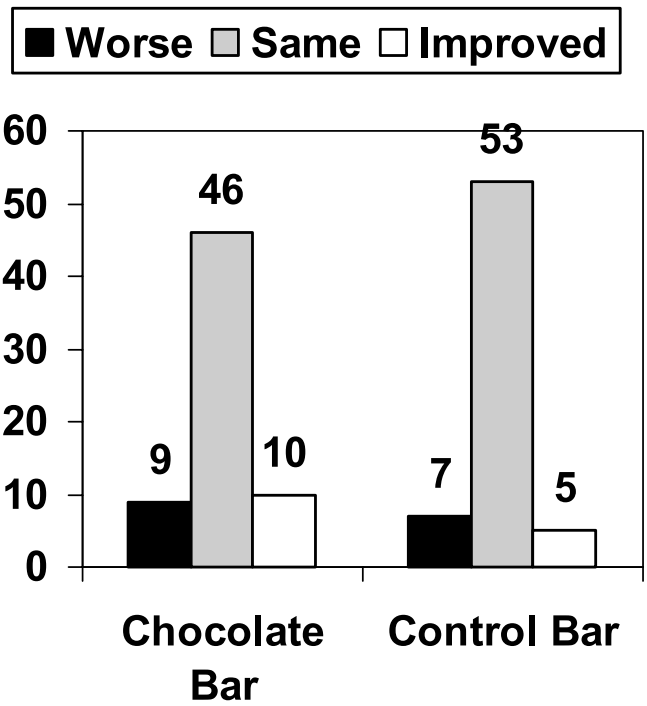

Figure 1 Effect of chocolate bar and control bar in acne incidence rates. Adapted from Fulton and co-workers.[12]

The Fulton and co-workers study[12] is frequently erroneously interpreted to mean that chocolate candy per se does not influence the development of acne. In fact, the treatment variable was not chocolate candy or even the bittersweet chocolate bar used in the study, but rather the specific ingredients within the bittersweet bar, the cacao solids (cocoa butter and cacao liquor), which were excluded from the manufacture of the control bar and replaced with partially hydrogenated vegetable fat (28% by weight). Both the control bar and the bittersweet bar contained high concentrations of sucrose (53% and 44.3% by weight, respectively). Cacao liquor (frequently called cacao paste) is derived from the ground core (nibs) of cacao seeds (*Theobroma cacao*), whereas cocoa butter is the fat extracted from cacao seeds. The only logical interpretation of this study is that cacao solids (cacao paste and cocoa butter) may not be involved in the etiology of acne. The results of the experiment cannot be generalized to assume that chocolate candy does not cause acne because chocolate candy contains many other ingredients in addition to cacao solids. For instance, milk chocolate candy typically contains 7 ingredients: (1) cacao paste; (2) cocoa butter; (3) sugar, usually sucrose; (4) nonfat milk solids; (5) milk fat; (6) an emulsifier, usually lecithin; and (7) flavoring, usually vanilla. Accordingly, any of the remaining ingredients in chocolate candy either individually or in combination with one another cannot be ruled out in the etiology of acne.

As has been previously pointed out,[14] both the treatment and control bars, because of their similar high sucrose contents, would have each elicited high glycemic and insulinemic responses as a result of their inherent high glycemic

loads.[17] Consequently, if these physiologic responses underlie the development of acne, then this experiment would not be able to resolve a treatment effect.

Other experimental design issues cloud the interpretation of this study. As with the Anderson study,[11] because the treatment and control bars were consumed in addition to the subjects' normal diet, there is no way of knowing how much total cacao solids were consumed either during the control or treatment arms of the experiment because no baseline measurements of the normal diet were made. Finally, because lesion counts were lumped into 1 of 3 ordinal categories, this approach could have lacked precision to determine a treatment effect. For example, a 25% increase in lesion counts may have been statistically significant, but would been classified as "unaffected" because of the arbitrary 30% cutoff point for each ordinal category.

In summary, neither the historical literature, nor the Fulton and co-workers[12] and Anderson[11] studies can be used as conclusive evidence for ruling out the role of diet in the pathogenesis of acne. The present consensus within the dermatology community that diet and acne are unrelated[1-8] has little or no factual support. In contrast, during the past 34 years since the publication of the last human diet/acne intervention,[11] a wealth of evidence has emerged showing that diet-induced changes in hormonal and cytokine homeostasis represent the most likely environmental factor underlying the development of acne.

Evidence Supporting the Role of Diet in Acne Pathogenesis

Over the course of the past 50 years, the major proximate causes of acne have been well-described.[15,18-21] Despite this knowledge, the following quote is representative of the state of affairs regarding acne's ultimate cause: "*despite* years of research, the basic cause of acne remains unknown. . ."[20] To understand how diet may influence the development of acne, it may be useful to first review: (1) the range of lesions within acne's umbrella designation, (2) the epidemiology of the disease, and (3) the widely recognized proximate causes of acne.

Lesion Description, Nomenclature, and Epidemiology

Acne lesions may be classified across a spectrum of morphologies with the following nomenclature and description: (1) open comedones 1 to 5 mm in diameter; (2) closed microcomedones ≤1 mm in diameter; (3) closed comedones 1 to 2 mm in diameter; (4) closed macrocomedones up to 5 mm in diameter; (5) superficial inflammatory pustules; (6) deeper inflammatory papules; (7) deep-seated small nodules, ie, 5-10 mm in diameter; and (8) deep-seated large nodules or abscesses (>10 mm in diameter). Most acne patients have a mixture of noninflammatory comedones and inflammatory papules, pustules, and nodules that can be classified to 1 of 3 levels of severity according to the International Consensus Conference Classification system: mild, ie, few-to-several comedones, papules, pustules, no nodules; moderate, ie, several to many comedones, papules, pustules, and few-to-several nodules; and severe, ie, numerous comedones, papules, pustules, and many nodules.[22]

In western industrialized societies, acne is a ubiquitous skin disease that affects between 40 to 50 million individuals in the United States.[23] Although it mainly afflicts adolescents, acne also is present in children and adults. Some degree of facial acne has been found in 54% of women and 40% of men older than 25 years of age.[24] In this same group, clinical facial acne afflicted 12% of the women and 3% of the men and persisted into middle age. Among pediatric populations the prevalence of acne increases with age. In 10- to 12-year-old children, 28% to 61% of the population has clinically diagnosed acne, whereas 79% to 95% of 16- to 18-year-old adolescents are afflicted.[25-27] Even a significant percentage of children (4-7 years) are diagnosed with acne.[26] In contrast, acne has been reported to be absent in nonwesternized populations such as the Inuit (ie, Eskimo),[28,29] Okinawa islanders,[30] Ache hunter-gatherers,[31] and Kitavan islanders.[31] Although familial studies[32] have demonstrated that hereditary factors are important in determining susceptibility to acne, the complete absence of this disease in nonwesternized populations points strongly to underlying environmental factors, including diet.[31]

Proximate Causes of Acne

Acne is believed to develop from the interplay of 5 major pathogenetic factors: (1) increased proliferation of basal keratinocytes within the pilosebaceous duct, (2) incomplete separation of ductal corneocytes from one another via impairment of apoptosis and subsequent obstruction of the pilosebaceous duct, (3) androgen-mediated increases in sebum production, (4) colonization of the comedo by *Propionibacterium acnes*, and (5) inflammation both within and adjacent to the comedo.[15,18-21]

Dietary Influence on Keratinocyte Proliferation and Corneocyte Desquamation

A crucial initial step in the formation of closed microcomedones is the obstruction of the pilosebaceous duct by corneocytes derived from the differentiation of basal keratinocytes. These corneocytes block the pilosebaceous orifice because they are overly adherent to one another and do not separate normally during desquamation.[18] Their increased cell-to-cell cohesion is caused by intact desmosomes[33-38] that normally would weaken and disintegrate via apoptosis during desquamation. Hence, an impairment of, or a delay in, the normal apoptotic process in corneocytes represents a fundamental mechanism underlying the formation of the microcomedo, the precursor lesion of acne. Additionally, increased proliferation of basal keratinocytes (which ultimately may become overly cohesive corneocytes) fuels the obstruction of the pilosebaceous duct.[39] A significant body of evidence now exists demonstrating that diet influences a number of hormones that regulate both keratinocyte proliferation and corneocyte apoptosis.

The glycemic index, originally developed in 1981, is a

Table 1 Glycemic Indices and Glycemic Loads of Various Food Groups

	Glycemic Index	Glycemic Load		Glycemic Index	Glycemic Load
Grain products			Vegetables		
Rice Krispie cereal[1]	82	72.0	Baked potato	85	21.4
Cornflakes[1,2]	81	70.1	Sweet potato	61	14.8
Rice cakes[3]	78	63.6	Yam	37	8.4
Shredded wheat cereal[4]	75	62.0	Rutabaga	72	6.3
Graham wafers[5]	74	56.8	Beets	64	6.3
Cheerio cereal[6]	74	54.2	Carrots	47	4.7
Rye crisp bread[7]	64	52.6	Fruits		
Vanilla wafers[5]	77	49.7	Banana	52	11.9
Stoned Wheat thins[5]	67	41.9	Grapes	46	8.2
Corn chips[8,9]	63	39.9	Kiwi fruit	53	7.5
Muesli bar[10]	61	39.3	Pineapple	59	7.3
Bagel	72	38.4	Apple	38	5.8
Doughnuts	76	37.8	Pear	38	5.7
White bread	70	34.7	Watermelon	72	5.2
Whole wheat bread	71	32.7	Orange	42	5.0
All bran cereal[12]	42	32.5	Dairy foods		
Sugar, sweets			Ice cream	61	14.4
Jelly beans	78	72.6	Yogurt, low fat	27	5.3
Lifesavers[11]	70	67.9	Skim milk	32	1.6
Table sugar (sucrose)	65	64.9	Whole milk	27	1.3
Mars bar[12,13]	65	40.4			

Glycemic load = (glycemic index × carbohydrate content in 100 g portions). The glycemic reference is glucose with a glycemic index of 100. Data adapted from Holt et al.[17]

[1]Kellogg's Inc., Canada; [2]Kellogg's Inc., New Zealand, Australia, U.S.A.; [3]Rice Growers Co-op, Australia; [4]Nabisco Brands Ltd., Canada; [5]Christie Brown and Co., Toronto; [6]General Mills Inc., Canada; [7]Ryvita Company Ltd., U.K., Canada; [8]Smith's Snack Food Co., Australia; [9]Old El Paso Foods Co., Canada; [10]Uncle Toby's, Australia; [11]Nestlé, Australia; [12]Mars Confectionery, Australia; [13]M & M Mars, U.S.A.

relative comparison of the potential of various foods or combination of foods to raise blood glucose, based on equal amounts of carbohydrate in the food.[40] In 1997, the concept of glycemic load (glycemic index × the carbohydrate content per serving size) was introduced to assess the potential of a food to raise blood glucose, based on both the quality and quantity of dietary carbohydrate.[41] Table 1 lists the glycemic indices and loads of various foods and demonstrates that refined grain and sugar products nearly always maintain much higher glycemic loads than unprocessed fruits and vegetables. From an endocrine perspective, the importance of the glycemic index and load is that they are closely related to the insulin response.[42]. An exception to this general rule is dairy products, which exhibit low glycemic indices and loads but paradoxically elicit high insulin responses similar to white bread.[43] Highly glycemic and insulinemic foods are ubiquitous elements in western diets and comprise 47.7% of the per capita energy intake in the United States (Fig. 2).[44]

Fig. 3 demonstrates that high glycemic meals in normal male subjects significantly ($P < 0.05$) elevate day-long plasma insulin concentrations. Further, numerous studies as summarized by Ludwig[46] and Liu and co-workers[47] establish that chronic consumption of high glycemic load carbohydrates may cause long-term hyperinsulinemia and insulin resistance. Insulin influences circulating concentrations of free insulin like growth factor I (IGF-1) and insulin like growth factor binding protein 3 (IGFBP-3), which in turn directly regulate keratinocyte proliferation and apoptosis.[48] Chronic and acute hyperinsulinemia simultaneously elevates free IGF-1 while reducing IGFBP-3.[49-55] Free IGF-1 directly stimulates basal keratinocyte proliferation, whereas IGFBP-3 inhibits basal keratinocyte proliferation irrespective of its IGF-1 receptor activity.[48] Hence, elevations in the free IGF-1/IGFBP-3 ratio promote keratinocyte proliferation through at least 2 primary pathways.

The development of hyperinsulinemia and insulin resistance elicits a pathological rise in serum concentrations of nonesterified free fatty acids (NEFAs),[56] which in turn has been shown to cause over expression of the EGF receptor.[57] For acne patients, consumption of low glycemic index diets

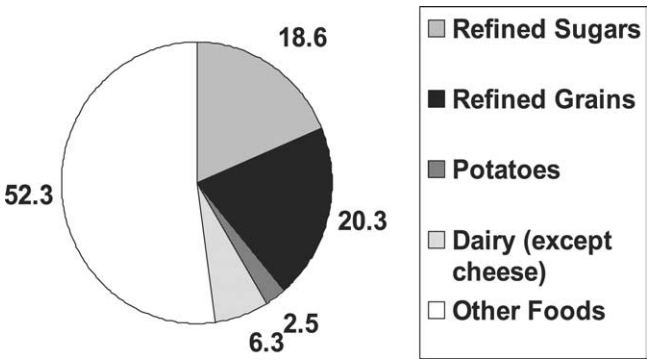

Figure 2 Per capita energy intake of high glycemic and insulinemic foods. Adapted from Gerrior and Bente.[44]

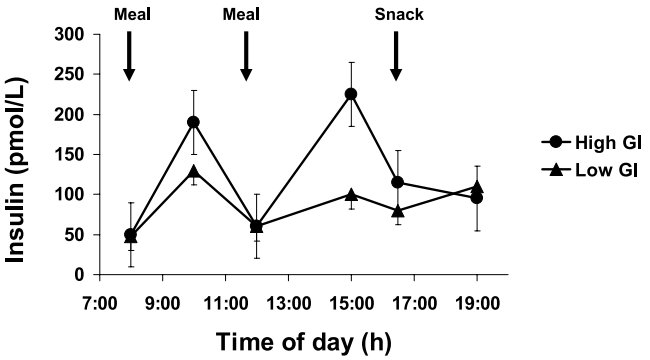

Figure 3 Influence of high glycemic meals and snacks on the day long concentrations of plasma insulin in 7 healthy male subjects. Adapted from Kiens and Richter.[45]

may be therapeutic not only because of their beneficial effects on insulin metabolism[46,47] but also because these diets are known to reduce plasma NEFA,[58] which may influence keratinocyte proliferation and differentiation via the EGF receptor pathway.[48]

IGFBP-3 is a potent proapoptotic factor in epithelial cells,[59] including keratinocytes.[48] As keratinocytes differentiate into terminal corneocytes, only basal keratinocytes produce IGFBP-3; however, serum-derived IGFBP-3 may influence localized concentrations of this hormone within differentiating corneocytes.[48] With regard to diet and acne, chronically elevated insulin concentrations in plasma may result in lowered IGFBP-3,[50] whereas ingestion of high glycemic meals acutely depresses IGFBP-3.[55] Accordingly, diet-induced lowering of IGFBP-3 represents a likely mechanism underlying the delay or impairment of apoptosis in corneocytes.

Further, IGFBP-3 is a ligand for the retinoid X nuclear receptor (RXR alpha) that along with other endogenous RXR alpha ligands (eg, *trans* retinoic acid and 9-*cis* retinoic acid) can operate in an additive manner to induce apoptosis.[59] Hence, the therapeutic effect of pharmaceutical retinoids in acne patients may function in part by restoring the RXR signal that was reduced by diet/insulin mediated reductions in IGFBP-3.

Dietary Influence on Androgen-Mediated Increases in Sebum Production

Sebum production is stimulated by androgens,[15,18-22] and, when excessive, can be pathogenetically involved in the development of acne. Accordingly, hyperinsulinemia may promote acne by its well-established androgenic effect. Both insulin and IGF-1 stimulate the synthesis of androgens in ovarian[60,61] and testicular[62,63] tissues. Further, insulin and IGF-1 inhibit the hepatic synthesis of sex hormone-binding globulin (SHBG),[64,65] thereby increasing the bioavailability of circulating androgens to tissues. Cross sectional studies have demonstrated inverse relationships between serum SHBG and both insulin[66] and IGF-1.[67-69] Additionally, sebum production is also stimulated by insulin[70] and IGF-1.[71] Direct injections of recombinant IGF-1 in humans elicit both androgenesis and acne lesion formation.[72] Higher serum androgen,[73] insulin[74] and IGF-1[75] concentrations may also be associated with the presence of acne in women. Taken together these data are suggestive that the endocrine cascade induced by diet-induced hyperinsulinemia enhances sebum synthesis and the development of acne.

Dietary Influence on Inflammation

The final factor involved in the pathogenesis of acne is inflammation of the dermis surrounding the 3 types of inflammatory acne lesions (papules, pustules, and nodules). Inflammation of the dermis is primarily thought to be caused by an immunological reaction to *P. acnes*, an anaerobic Gram-positive bacterium, which colonizes the sebum-rich environment of the closed comedo.[76] Certain agents (peptidoglycan–polysaccharides) within the cell wall of *P. acnes* may directly induce the expression of proinflammatory cytokines (tumor necrosis factor alpha, interleukin [IL]-1β, and IL-8) from peripheral blood monocytes (PBMs) in a dose-dependent manner.[76] Increased concentrations of these cytokines can stimulate other inflammatory mediators, including prostanoids and leukotrienes. It has been suggested that overproduction of inflammatory cytokines by PBMs in response to *P. acnes* may underlie the development severe inflammatory acne.[76]

Increased expression of the inflammatory cytokine IL-1α also may promote the development of acne by adversely influencing keratinocyte terminal differentiation.[18] Elevated concentrations of IL-1α in isolated follicular infundibula resulted in hypercornification and scaling similar to the initial events of microcomedogenesis.[79]

Diet is a well-known modulator of the systemic inflammatory response. One of the most important dietary factors that influence inflammation is the relative intake of ω- 6 and ω-3 polyunsaturated fatty acids (PUFAs).[80] The typical western diet maintains a significantly higher concentration of ω-6 PUFAs at the expense of a lowered ω-3 PUFAs because of the predominance of ω-6 PUFAs in most vegetable oils and processed foods made with these oils.[80] In the current US diet, the ratio of ω-6/ω-3 PUFA has risen to 10:1,[81] whereas in nonwesternized diets it has been estimated between 2 to 3:1.[82] Accordingly, the average western diet promotes a proinflammatory cytokine and eicosanoid profile that underlies the development of a variety of inflammatory disorders.[80]

For the acne patient, increased consumption of dietary ω-3 PUFA may be therapeutic because of their ability to suppress inflammatory cytokine production. Supplementary intake of ω-3 fatty acids has been shown frequently to suppress IL-1β,[83-86] IL-1α,[83,88] tumor necrosis factor-α,[83-88] Il-6,[84,86,88] and IL-8[88] in PBMs. The suppression of IL-1α by dietary ω-3 PUFAs may positively influence corneocyte differentiation by preventing or attenuating the hypercornification and scaling that occurs during microcomedogenesis. Additionally, dietary ω-3 fatty acids are also known to inhibit synthesis of the proinflammatory eicosanoids prostaglandin E_2 and leukotriene B_4.[85] Because a recent study demonstrated that an leukotriene B_4 blocker led to a 70% reduction in inflammatory acne lesions,[89] similar beneficial effects would be expected

with dietary increases in ω-3 PUFA along with reductions in ω-6 PUFAs.

Corroborative Evidence Linking Insulin Metabolism and Acne

Tolbutamide was one of the first sulfonylurea drugs used to successfully treat patients with type 2 diabetes. One of the unexpected side benefits was that it also was shown to be therapeutically effective in treating acne in otherwise-healthy patients. Most,[90-93] but not all,[94] studies performed during the 1950s and early 1960s reported significant improvement in acne symptoms with tolbutamide. Surprisingly, interest in tolbutamide and acne waned in the early 1960s, and no modern well-controlled studies have followed up on these earlier experiments. Further, tolbutamide's therapeutic mode of action in acne patients remains unknown; however, it is likely that it is linked to the improved insulin homeostasis that occurs with tolbutamide.[95]

Acne is a characteristic feature in patients with polycystic ovary syndrome (PCOS), who are also frequently obese, hyperinsulinemic, insulin resistant, and hyperandrogenic.[96] These patients typically maintain elevated serum concentrations of androgens, IGF-1, and lower concentrations of SHBG.[96-98] Androgen levels can be lowered and disease symptoms alleviated by improving insulin sensitivity through weight loss[99] or by use of pharmaceuticals such as metformin,[100] which improve insulin metabolism. Both metformin[101] and pioglitazone (a new insulin-sensitizing agent belonging to the thiazolidinedione class which binds the PPAR-γ receptor)[102] have been demonstrated specifically to improve acne symptoms in patients with PCOS. Metformin[103] and pioglitazone[104] not only improve insulin metabolism but result in a depression of adrenocorticotropic hormone-stimulated androgen production in women with PCOS. Both of these physiological changes would be therapeutic for acne patients. To date, no clinical trials evaluating these pharmaceuticals in acne patients without PCOS have taken place.

Insulin resistance and obesity are not only well-recognized symptoms in patients with PCOS[96] but also typically occur in non-PCOS patients as well.[47] Hence, because of the concurrent presence of insulin resistance with obesity, it might be expected that acne incidence may be more prevalent in the obese. No modern epidemiological studies have examined this relationship; however, a single older study noted a significant relationship between obesity and acne.[105]

Dietary interventions using low glycemic load carbohydrates may have therapeutic potential in the treatment of acne because of the beneficial endocrine effects these diets possess. A large interventional study has demonstrated that diets rich in low glycemic foods reduced serum testosterone and fasting glucose while improving insulin metabolism and increasing SHBG.[106] These endocrine changes are consistent with those known to promote normal follicular cell proliferation and to reduce sebum production.

Conclusion and Recommendations

The last diet-acne trial was published in 1971.[11] In the ensuing 34 years, great strides have been made in understanding how diet influences long-term health and well being. Unfortunately, appreciation of this information has generally gone unnoticed in the dermatology community, as witnessed by the 34-year vacuum since the last dietary intervention in acne patients. A substantial body of literature now exists that directly implicates diet as the most likely environmental factor underlying the development of acne. Confirmation of the diet-acne hypothesis will require numerous well controlled dietary interventions examining multiple nutritional factors.

As a starting point, future experiments testing the diet–acne hypothesis should employ diets that mimic the nutritional characteristics of diets found in nonwesternized populations known to be free of acne.[31] Although there is no single nonwesternized diet, there are certain universal characteristics that have a theoretical basis for testing. These diets are free of processed foods, cereal grains, dairy products, refined sugars, and refined oils and almost entirely comprise unprocessed fresh, fruits, vegetables, and lean meats, fish, and seafood.

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