INCIDENCE, PREVALENCE, AND PATHOPHYSIOLOGY OF ACNE*

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ABSTRACT

Acne is the most common dermatologic condition encountered in clinical practice, affecting nearly all adolescents and young adults to some degree. The pathophysiology of acne is complex. Increased sebum production by sebaceous glands and abnormal desquamation of hair follicles occur in response to increasing androgen levels with the onset of puberty. Obstruction of follicles causes follicular distention, which is often accompanied by the proliferation of the bacteria Propionibacterium acnes and the activation of an inflammatory response. Although the diagnosis of acne is usually straightforward, some conditions are occasionally confused with acne, including periorificial dermatitis, keratosis pilaris, angiofibromas, bacterial folliculitis, and demodex folliculitis. In addition to physical discomfort, acne is associated with considerable psychological distress, limitation of activities, and increased risk of depression and suicide. The relationship between acne and diet is controversial. Some studies have demonstrated that diets that are high in minimally processed plant or animal foods or low in highly processed carbohydrates are associated with lower rates of acne, although other studies have failed to demonstrate important differences in diet between subjects with and without acne. Recent research suggests that some dairy products may increase acne risk during adolescence. (Adv Stud Med. 2008;8(4):100-105)

Acne vulgaris is the most common skin condition that is treated by physicians, accounting for more than 14 million office visits per year. Acne typically appears for the first time during early adolescence, and is present to some degree in approximately 85% of individuals between the ages of 15 and 17 years.1 The first acne lesions often appear before the emergence of secondary sexual characteristics, and are one of the earliest signs of impending puberty. Acne presents several significant challenges, including a complex etiology, concerns about antibiotic resistance, and the potential for scarring. The effects of acne are not limited to the skin—acne lesions among adolescents and young adults generally occur at a time of heightened emotional sensitivity, and may contribute to significant psychological distress, depression, and even increased risk of suicide.

ACNE PATHOPHYSIOLOGY AND CLINICAL PRESENTATION

The pathophysiology of acne is a multifactorial process that begins with the obstruction of the piloseba-
ceous unit, which consists of the hair follicle, hair shaft, and sebaceous gland. Acne lesions are therefore concentrated in areas of greatest sebaceous gland density, including the face, neck, chest, upper arms, and back. Usually beginning at approximately 8 to 9 years of age, increased production of adrenal androgens stimulates the secretion of sebum—a waxy substance containing a mixture of wax and sterol esters, triglycerides, cholesterol, and potentially inflammation-inducing free fatty acids—by the sebaceous glands.

Sebum secretion is accompanied by increased production of squamous cells lining the follicle, increased adhesion of follicular epithelial cells to one another, and abnormal keratinization of the follicle inner surface. The accumulation of sebum, epithelial cells, and keratin obstructs the follicle, causing the formation of a keratin plug and follicle swelling, resulting in the formation of a microscopic lesion (the microcomedone) below the skin surface (Figure 1). The microcomedone is the earliest acne lesion, and is common to inflammatory and noninflammatory acne.

Enlargement of the keratin plug and continued swelling of the follicle result in the formation of a visible comedone, which is the basic acne lesion. A comedone may have a widely dilated opening to the skin surface (an open comedone or blackhead), or an opening that is only microscopic (a closed comedone or whitehead). Although the dark coloration of the blackhead is believed by many patients to be caused by dirt, it actually reflects the oxidation of compacted epithelial cells and sebaceous lipid. Inflammatory acne occurs when the follicles become colonized by Propionibacterium acnes, a gram-positive anaerobe that is part of the normal skin flora. The proliferation of P. acnes stimulates the infiltration of immune cells (eg, CD4 T lymphocytes and neutrophils), which disrupt the follicular wall and cause the dispersal of lipids, cellular components, and bacteria into the surrounding dermis. Cytokines, peptides, and other inflammatory mediators released during this process stimulate a localized inflammatory response, resulting in papule formation. A more intense inflammatory response results in the formation of pustules, which are often accompanied by overlying comedonal acne. Larger inflammatory lesions may result in the formation of cysts. Nodules are deeper lesions that often involve more than 1 follicle and are associated with a high likelihood of scarring.

Typical clinical presentations of acne are depicted in Figures 2 and 3. Comedonal acne is shown in Figure 2, including open and closed comedones on the patient’s chin. Inflammatory acne is illustrated in Figure 3. As described in more detail later in this monograph, postinflammatory dyspigmentation or hyperpigmentation often occur following acne healing, especially in patients of color. Finally, scarring is a common complication of acne that may be prevented by early treatment.

The diagnosis of acne is usually straightforward, although some conditions may occasionally be confused with acne. Periorificial dermatitis is a common acneiform disorder in children and young adults that is generally thought to represent a pediatric form of acne rosacea. Previously referred to as perioral dermatitis,

Figure 1. Types of Acne Lesions

this condition is characterized by papules and pustules, typically without comedones, that are usually distributed near the eyes, nose, and mouth. Keratosis pilaris, a common disorder in pediatric dermatology practice, is characterized by hyperkeratotic papules associated with hair follicles, typically involving the cheeks, outer arms, and dorsal thighs. This condition is especially likely to be confused with acne when it is inflammatory. Keratosis pilaris is very difficult to treat, and should be regarded as a skin type rather than a disorder.

Angiofibromas (formerly referred to as adenoma sebaceum) are encountered in the setting of tuberous sclerosis, an autosomal dominant multiple hamartoma syndrome. These papules may resemble acne, but are typically translucent (resembling molluscum), are located in the midfacial region, generally appear earlier than acne (typically at approximately 4–6 years of age), and are not accompanied by comedones. Bacterial folliculitis may cause erythematous papules and pustules that are rarely mistaken for acne. These lesions typically involve the buttocks and posterior thighs of diaper-wearing children, although they may also appear in other locations. Other forms of folliculitis are sometimes confused with acne. For example, pityrosporum is often associated with truncal papules in immunosuppressed patients. This disorder may be distinguished from acne by the absence of facial lesions and by a positive potassium hydroxide (KOH) test result.

Demodex folliculitis is also sometimes encountered in individuals with immunosuppression, presenting as a persistent acne-like eruption on the face that does not respond to acne therapy. The presence of demodex mites may be confirmed by a skin surface biopsy. Treatment with topical permethrin or sulfa-based antibiotics is usually effective for these patients. Finally, milia is unlikely to be confused with acne, although the characteristic white papules on a background of noninflamed skin may resemble closed comedones. These lesions tend to occur sporadically during childhood, especially at sites of abrasional trauma, presenting as clusters of white papules with a total absence of inflammation. They may rarely be syndrome associated.

The emotional impact of acne is often very difficult for patients to tolerate. Adolescents are in a period of life that is characterized by pronounced emotional volatility, and they are often especially sensitive to the effects of acne or other conditions that adversely affect their physical appearance. As a result, acne often causes significant anxiety, depression, frustration, and
anger. Approximately 7% of patients with acne exhibit depression or suicidal ideation. Impairments in functional ability have been observed in several settings, including socializing with friends, dating, participating in sports, and academic attainment. Individuals with moderate-to-severe acne are also at increased risk of unemployment. In addition to the emotional difficulties associated with acne in adolescent patients, these individuals also tend to expect improvement very quickly, and they are often impatient with and poorly adherent to acne therapy. Education about the time required for acne therapy to work is especially important for these patients, accompanied by regular follow-up visits with positive reinforcement whenever possible. As described in the article by Dr Hebert, acne therapy typically employs a combination of treatments to reduce acne lesions and avoid antibiotic resistance.

**The Relationship Between Acne and Diet**

There are several common misconceptions about the causes or treatment of acne. Many people think that acne is caused by dirt, and that intensive scrubbing of the skin can cure acne. However, vigorous scrubbing or abrasive cleansers do not improve acne, and may actually worsen it by traumatizing the skin and exacerbating inflammation. The relationship between acne and diet is controversial. Acne is often attributed to several dietary causes, including chocolate, soda, sweets, or fried foods, although many acne experts have argued that diet is not a significant contributor to acne.

A relationship between acne and glycemic load was initially suggested by the observation that the prevalence of acne is relatively low in some nonwesternized societies, and that acne becomes more common when previously isolated societies adopt westernized diets. In particular, researchers have noted that acne is nearly absent in regions where the diet consists primarily of minimally processed plant or animal foods and very low amounts of western-style high-carbohydrate foods that yield very high glycemic loads when ingested. For example, Cordain et al examined the prevalence of acne in 2 non-westernized populations—Kitavan islanders of New Guinea and the Ache hunter-gatherers of Paraguay. In New Guinea, dermatologic examination revealed no cases of acne among a total of 1200 subjects, including 300 subjects between the ages of 15 and 25 years. Of 115 subjects in Paraguay, no cases of acne were identified over a follow-up period of more than 2 years. It has been suggested that increasing glycemic load modulates acne risk by altering serum insulin concentration and the production of insulin-like growth factor-1 (IGF-1), a mitogen that may stimulate follicle growth.

Test subjects from New Guinea have been shown to exhibit low serum insulin concentrations and high insulin sensitivity, in contrast to hyperinsulinemia and insulin resistance that are more commonly encountered in association with westernized high-carbohydrate diets. Diet-related hyperinsulinemia may also contribute to acne by stimulating androgen production. Smith et al recently conducted a randomized study to evaluate the effect of a low–glycemic-load diet on acne in male subjects between 15 and 25 years of age. A total of 43 subjects were randomly assigned to 1 of 2 dietary treatment groups for 12 weeks. Subjects in 1 group consumed a low–glycemic-index diet consisting of 25% energy from protein, 30% from fats, and 45% from carbohydrates with low glycemic index values. Subjects in the control group consumed a diet

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**Evidence-Based Practice Recommendation**

**I. Practice Recommendation:** The pathogenesis of acne is multifactorial and includes hormonal, microbiological, and immunological mechanisms. Combination therapy should be used to target as many pathogenic factors as possible. Topical antibiotics alone may increase the risk of antibiotic resistance. Patients who require topical antibiotic therapy should be treated with benzoyl peroxide in combination with erythromycin or clindamycin.

**Name of AAFP-Approved Source:** American Academy of Dermatology: Guidelines of Care for Acne Vulgaris Management.

**Specific Web Site of Supporting Evidence from Approved Source:** [http://www.aad.org/pm/science/_docs/ClinicalResearch_Acne%20Vulgaris.pdf](http://www.aad.org/pm/science/_docs/ClinicalResearch_Acne%20Vulgaris.pdf).

**Strength of Evidence:** A group of experts in the management of acne, convened by the American Academy of Dermatology, reviewed the clinical evidence supporting various acne management strategies. The authors identified several reports demonstrating that combinations of benzoyl peroxide and a topical antibiotic reduce or eliminate antibiotic resistance, and that combination therapy is more effective than either individual treatment alone.
high in carbohydrate-dense foods similar to their baseline diets. After 12 weeks, subjects in the low–glycemic-index diet group exhibited a greater reduction from baseline than the control subjects for both inflammatory lesion counts and total lesion counts (Figure 4). The dietary intervention was also associated with reduced circulating insulin and improved insulin resistance, in addition to reduction in the free androgen index and an increase in IGF-binding protein. However, other studies have found no significant differences in several metabolic factors between individuals with or without acne vulgaris, including serum glucose, insulin, glycemic index, or self-reported dietary glycemic load.

The relationship between acne and the consumption of dairy products and other foods was examined using data from the Nurses’ Health Study II, a long-term, ongoing prospective study that is examining associations among several lifestyle factors and illnesses among women who were between the ages of 25 and 42 years when the study began in 1989. These investigators retrospectively evaluated data from 2 questionnaires that were provided by more than 47 000 women. One questionnaire asked the participants about their diet during their high school years, and the second questionnaire asked the subjects whether they had a lifetime history of physician-diagnosed acne. A history of physician-diagnosed acne was significantly associated with self-reported high-school milk intake, but only among women who had regularly consumed skim milk.

Acne was also significantly associated with more frequent consumption of several other dairy products, including instant breakfast drink, sherbet, cream cheese, and cottage cheese. Physician-diagnosed acne was not significantly associated with patient-reported intake of other foods that have been associated with

**Figure 4. Effects of a Low–Glycemic-Load Diet on Acne Vulgaris**

*Mean (±SEM) percentage changes from baseline in inflammatory acne lesion counts and in total acne lesion counts in the low–glycemic-load group (solid line; n = 23) and the control group (dashed line; n = 20) at each visit. Repeated-measures analysis of variance was performed by incorporating the absolute data (log transformed) from each follow-up visit, with baseline counts as the covariate.*

acne, including chocolate, soda, pizza, and French fries. The authors noted that milk contains numerous proteins that might potentially influence acne risk, including estrogens, progesterone, androgens and androgen precursors, IGF-1, and others. They also hypothesized that differences in processing between whole milk and skim milk might affect acne risk by altering the bioavailability of some of the hormonal components of milk. For example, they noted that whole milk contains more estrogen than skim milk, and that estrogens may exert a protective effect against acne. Although these results provide some evidence for an association between acne and the consumption of dairy products during adolescence, a significant limitation of this study was that it relied entirely on participants’ retrospective recall of diet and acne diagnosis.

CONCLUSIONS

Acne is a common disorder that is associated with considerable patient distress, anger, and depression. The pathophysiology of acne involves a series of complex interactions between hormones, alterations to keratinization of the sebaceous glands, and bacterial infection. For the past 2 decades, most acne specialists have argued that there is no clear association between acne and foods, such as chocolate or other sweets. Some newer studies have suggested that acne may in fact be linked to diet, although the benefits of dietary modification to reduce the incidence or severity of acne are not well established at present.

REFERENCES