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OTC Products for the Treatment of Acne

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Acne vulgaris is a common skin disorder, affecting 40 to 50 million people in the United States.[1] Approximately 85% of the adolescent population will develop acne to some degree, and 40% to 54% of individuals older than 25 are affected as well. The incidence is generally universal among ethnicities and between genders, except in the case of adult acne; approximately 3% of males are affected versus 12% of females.[2] Although acne is a self-limiting disorder that may appear to be mostly cosmetic in nature, it may place an emotional and psychological burden on the affected individual that is more than skin deep. The physical change on the surface of the skin and, at times, the accompanying scarring may lead to a reduction in quality of life comparable to that of people with epilepsy, asthma, diabetes, or arthritis.[3] The psychologic impact, which can include social withdrawal, lack of confidence, anxiety, and depression, has been associated with higher rates of unemployment. [1,3,4]

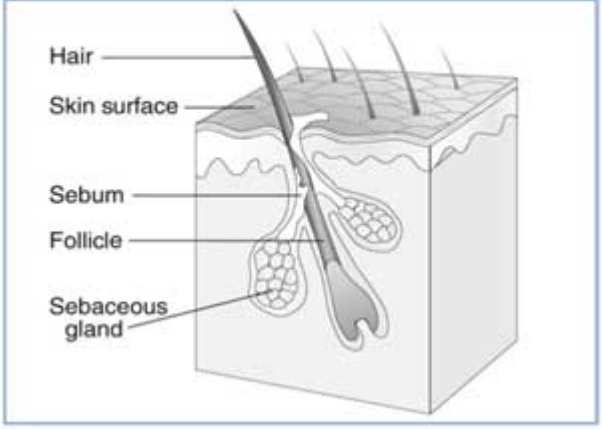
In the U.S., the direct cost of acne is estimated to be $1 billion per year; $1 million is spent on OTC products.[4] Considering the extensive marketing of these products and the implications of increased self-confidence and clearer skin, the number of available products is not surprising. Although 20% of all visits to dermatologists are for the evaluation of acne, there are many patients who purchase OTC products to clear and treat their acne.[2] Therefore, pharmacists have an important role in evaluating the patient; choosing the best OTC therapeutic regimen, if appropriate; and counseling the patient about necessary nonpharmacologic measures.

Pathogenesis of Acne

Acne is a disease of the pilosebaceous units, which are found everywhere in the dermis (**Figure 1**) except the palms and soles.[5] The face, upper back, and chest have the highest density of these units. Each unit consists of a

hair follicle and sebaceous gland that produces sebum, an oily substance containing free and esterified fatty acids and lipid components. There are four primary factors involved in the pathogenesis of acne: increased sebum production, abnormal keratinization of follicles, *Propionibacterium acnes* proliferation, and inflammation (**Table 1**). The interplay of these four factors causes the formation of acne lesions. The amount of sebum secreted may correspond to the severity of acne. Sebum production is stimulated by androgen circulation, and during puberty, there is increased androgenic activity. The increase in sebum, combined with increased sloughing of keratinocytes (cells lining the follicle) and hair, produces a plug in the narrow follicle. *P acnes* normally resides on the dermis; however, the mixture of sebum and cells provides the bacterium with an environment that facilitates proliferation in the plugged follicles. This in turn may cause inflammation, a consequence of the bacteria producing biologically active mediators and promoting proinflammatory cytokine release.[1,2,5-7]

FIGURE 1
NORMAL PILOSEBACEOUS UNIT



Source: Reference 5.

External factors that exacerbate acne include high humidity; local irritation/friction (e.g., occlusive clothing, headbands, hand resting on face); dirt, vaporized cooking oils, chemicals; oil-based cosmetics/hair products; moisturizers/tanning oils with comedogenic oils (i.e., lanolin, mineral oil, cocoa butter); medications (i.e., phenytoin, isoniazid, phenobarbital, lithium, steroids, some oral contraceptives); and diet (high-glycemic carbohydrates possibly lead to hormonal change).[2,6] Internal factors that exacerbate acne include prolonged sweating, emotions (i.e., stress), hormones (associated with menses), and heredity.[2]

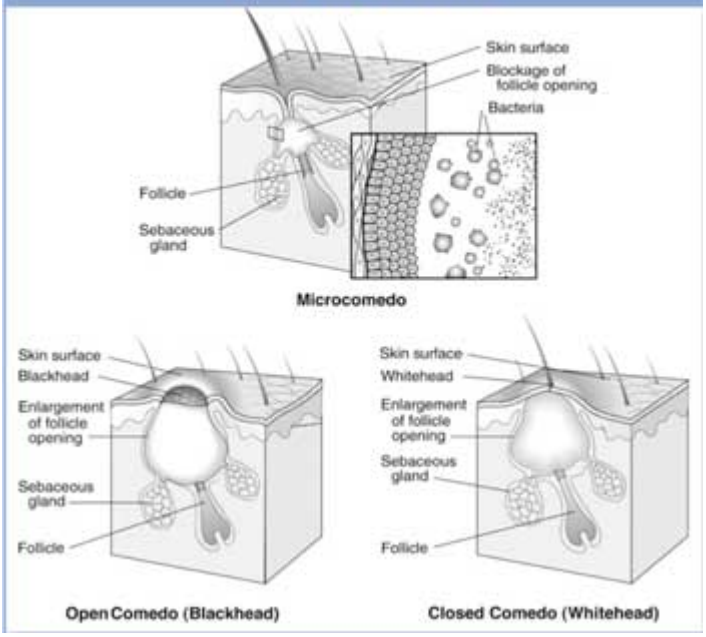
TABLE 1
PATHOGENESIS OF ACNE

Pathogenic Factor	Mechanism	Effect
Increased sebum production	Stimulated by androgen (enhanced during puberty)	Increased sebum onto skin surface
Abnormal keratinization of follicular epithelium	Increased sloughing of keratinocytes and sebum, cause follicle to plug	Comedo formation; favorable environment for *Propionibacterium acnes*
Growth of *P acnes*	Normal flora proliferate in plugged follicles	Trigger immune responses and proinflammatory cytokine release
Inflammation	Secondary to biologically active mediators produced by bacteria	Papule or pustule formation

Clinical Presentation

Clinically, acne presents as lesions that may be noninflammatory comedones, either open or closed, or inflammatory pustules, erythematous papules, cysts, nodules, or abscesses (**Figure 2**). The initial lesion is the closed comedo, an enlarged and plugged hair follicle remaining beneath the skin, more commonly known as a *whitehead*. An open comedo, known as a *blackhead* , occurs when the contents of the follicle extrude. Rupturing of the follicular wall may cause a more severe inflammatory reaction, discharging the contents into the surrounding tissue. This would present as *papules* (i.e., small, pink bumps on the skin) or *pustules* (i.e., white or yellow pus filled papules that may be red at the base). More painful solid lesions called *nodules* or deep pus-filled lesions called *cysts* may occur and are more likely to leave scarring.

FIGURE 2
TYPES OF LESIONS



The diagnosis of acne is not difficult and is often made by the patient. Acne is characterized by a variety of lesions, particularly on the face but also on the neck, chest, shoulders, and back. Various systems are utilized to classify the severity of acne, which take into account the number, type, and distribution of comedones, papules/pustules,

and nodules. The severity of acne can range from mild to severe. Detailed description of the various grades of acne is described in **Table 2**. Knowing the degree of severity allows the pharmacist to evaluate the necessity of immediate referral to a physician and choose the appropriate OTC therapy.[2,4,7]

TABLE 2
CLASSIFICATION OF ACNE

Severity	Description
Mild	<10 papules/pustules; comedones, localized on one portion of face
Moderate	10-40 papules/pustules/comedones; mild lesions on trunk
Moderately Severe	40-100 papules/pustules/comedones; <5 larger, deeper nodules; face, chest, and back affected
Severe	Nodulocystic acne; painful and large lesions, with smaller papules/pustules/comedones

Treatment

The treatment of acne involves a combination of both nonpharmacologic and pharmacologic therapies.

Nonpharmacologic Therapy

Nonpharmacologic methods for preventing and treating acne include avoiding/minimizing exacerbating factors--such as restrictive clothing, resting hands on the face and/or skin, using oil-based cosmetics, infrequent washing of oily hair, exposure to environmental factors (i.e., dirt, chemicals)--and picking/squeezing acne lesions.[2] Patients should gently wash the face twice daily to remove excess sebum from the skin. Cleaners with pumice, polyethylene, or aluminum oxide may irritate the skin, producing inflammatory lesions, and should be avoided. In addition, antimicrobial soaps should be avoided, since they have no proven clinical value.

Pharmacologic Therapy

Benzoyl peroxide, salicylic acid, sulfur, sulfur with resorcinol, and several herbal remedies are available OTC to treat mild-to-moderate acne. There are numerous products bearing different names, dosage forms, and advertising claims; however, most contain one or more of the aforementioned active ingredients. Mechanistically, these various agents target the four pathogenic factors. A product should be chosen based on maximum efficacy with minimal adverse effects, as well as on targeting of the pathogenic factor.[8] Because patients have differing skin types, the dosage form achieving the greatest effect will vary among patients. **Table 3** provides information on selecting the appropriate dosage form for different skin types.

TABLE 3
HOW TO CHOOSE THE APPROPRIATE TREATMENT VEHICLE

Skin Type	Treatment Vehicle	Comments
Sensitive/dry skin	Cream	Nonirritating, nondrying
Oily skin	Gel	Drying effect; certain kinds of cosmetics may not adhere to gel; may cause burning irritation
	Solution	Mainly used with topical antibiotics
Any type	Lotion	Spread well over hairy areas; contains propylene glycol, which has burning/drying effects

Source: Reference 9.

Benzoyl Peroxide: Introduced in the 1960s, benzoyl peroxide is the most widely used topical agent for acne. It is available in various dosage forms in concentrations of 2.5% to 20%. The maximum concentration available as an OTC product is 10%. Benzoyl peroxide† has anti-inflammatory properties and is a bactericidal agent that penetrates the dermis and enters the pilosebaceous follicle, generating free radicals that oxidize proteins in the bacterial cell membrane and thereby reduce *P acnes.* Studies have shown that the various strengths of benzoyl peroxide have similar effectiveness; however, at equivalent strengths, the gel form is superior to the lotion form, because the drying effect of the alcohol in the gel enhances its effectiveness. Although *P acnes* has demonstrated resistance to antibiotics, its resistance to benzoyl peroxide has not been reported. Additionally, benzoyl peroxide has comedolytic effects due to irritation of the skin, which causes an increased rate of sloughing of epithelial cells. The comedolytic effect does not occur with washes and cleansers.[2,9-12]

Adverse reactions include excessive dryness, peeling, skin sloughing, erythema, and edema. These effects may be reduced by using a lower strength of benzoyl peroxide. A transient stinging or burning may occur. Additionally, bleaching of hair, clothing, and bed linens may occur with the use of benzoyl peroxide.[2]

The FDA is determining the safety of benzoyl peroxide. Warning statements have reported that benzoyl peroxide is a tumor promoter and progressor, and safety studies are being conducted to determine if it enhances ultraviolet radiationñinduced skin cancer. Studies conducted in the late 1990s concluded that benzoyl peroxide "is not carcinogenic in the skin or in ëselect internal organs' of mice and rats [and] does not enhance photocarcinogenesis in mice."[2]

The active ingredient in two parts of the three-step regimen of a popular product, Proactiv, is benzoyl peroxide 2.5%. One study compared the efficacy of Proactiv with benzoyl peroxide plus allylamine to possibly amplify effectiveness. Results indicated that the benzoyl peroxide/allylamine combination was more effective than Proactiv. Although this was a small-scale, open-label study, findings suggest that benzoyl peroxide activity may be augmented with a tertiary amine such as allylamine.[13]

Pharmacists should advise patients that benzoyl peroxide is associated with increased sun sensitivity; therefore, sunscreen should be thoroughly applied and reapplied as needed. Additionally, benzoyl peroxide should be applied

to dry skin once or twice daily. Before titrating the dosage or deeming the product ineffective, patients should keep in mind that maximum effects are seen in four to six weeks.

Salicylic Acid: Salicylic acid is a mild comedoyltic agent that acts as a surface keratolytic. It is a lipid-soluble beta hydroxy acid that may penetrate sebum-plugged pores. It is available in concentrations of 0.5% to 2% and is considered second-line treatment. Salicylic acid is found in many body washes and cleansers, as well as in topical creams and gels. Generally, the body washes and cleansers are not very effective, because the contact time on the skin is short. Adverse effects include transient stinging or burning of the skin, as well as redness or irritation.

Sulfur and Sulfur-Resorcinol: Precipitated or colloidal sulfur is a keratolytic and antibacterial agent utilized to treat acne in concentrations of 3% to 10%. Sulfur 3% to 8% may be combined with resorcinol 2% to increase the effect of sulfur. Possible disadvantages of these products include the noticeable color and odor of sulfur, as well as the possible dark brown scaling caused by resorcinol on darker skin (reversible). In addition, these products may be comedogenic when used consistently and therefore are better utilized for short-term spot treatment.

Herbal Products: There are several herbal products that may be effective in treating acne. Common ingredients in these products include alpha hydroxy acids, such as glycolic acid; tea tree oil; bovine cartilage; guggul; *Saccharomyces boulardii*; and zinc. Glycolic acid, in concentrations of 70%, may be used in face peels, significantly improving atrophic acne scars, while a concentration of 15% is moderately effective as a daily lotion or face wash. When tea tree oil 5% was compared to benzoyl peroxide 5%, it was found to significantly reduce the number of inflammatory lesions and comedones. Benzoyl peroxide was statistically superior in reducing the lesions and had a faster onset of action; however, tea tree oil was associated with fewer side effects. Tea tree oil may have a place in therapy for patients who are unable to tolerate the adverse effects of benzoyl peroxide. Oral zinc has been studied for the treatment of acne, since research has suggested lower serum and skin zinc levels in patients with acne. Small clinical trials show zinc to be favorable, but no conclusive data have yet emerged.

Homeopathic formulations include Acne by Nature's Sunshine, Acne Formula by HERBALmax, and Acne Support Combo by Traditional Tibetan Healing Inc. These formulations consist of a combination of various ingredients with insufficient evidence for effectiveness.[14]

Role of the Pharmacist

Pharmacists play a vital role in evaluating the patient. This includes obtaining medical/medication history, observing the number and types of lesions, referring patients to a physician if needed, choosing the appropriate therapeutic regimen, and counseling the patient. To achieve maximal benefit, patients need to be educated about the goals of treatment, realistic expectations, length of therapy, appropriate use of products, and the importance of adhering to the regimen. Many patients may be able to treat their acne utilizing OTC medications; however, it is imperative that the pharmacist know which patients to refer to a doctor. Patients should be referred to a physician if any of the following are noticed: moderate-to-severe acne (characterized by papules, pustules, cysts, scarring,

nodules), exacerbating factors (e.g., medications), differential diagnosis (e.g., rosacea, which occurs more often in women and is usually characterized by papules, pustules, redness on the central portion of the face into the scalp, and sensitivity to touch and sunlight; onset is usually between ages 20 and 60),[15] resistance or allergy to OTC treatment, and psychological effects.

Conclusion

Acne vulgaris is a common skin disorder, at times inflicting both physical scarring and emotional/psychological effects. It is usually self-diagnosed and self-treated. Although the patient is able to buy many of these products based on marketing and labeling, the most effective treatment regimens are individually developed, and include both pharmacologic and nonpharmacologic measures. At times, OTC treatments may be utilized in conjunction with prescription products to treat acne. The pharmacist is a great source for appropriate product selection and educational and empathetic counseling.

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