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## **Managing Adolescent Acne : A Guide for Pediatricians**

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*Pediatrics in Review* 2005;26;250

DOI: 10.1542/pir.26-7-250

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# Managing Adolescent Acne: A Guide for Pediatricians

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Author Disclosure  
Dr Krowchuk did not disclose any financial relationships relevant to this article.

**Objectives** After completing this article, readers should be able to:

1. Review the epidemiology and causes of adolescent acne.
2. Recognize the types of acne lesions and assess the severity of acne.
3. Design an appropriate treatment plan for adolescents who have acne.
4. Discuss the indications for use and adverse effects of topical and systemic agents employed in acne therapy.

## Introduction

Acne vulgaris, known simply as “acne,” is a chronic condition that may last for years and cause emotional distress and permanent scarring. Although acne has no cure, medications can control the disease and limit or prevent scar formation.

## Epidemiology

Acne is the skin disease most commonly treated by physicians. It is estimated that 17 million Americans have acne, including 85% of adolescents ages 15 to 17 years. In 2000, the most recent year for which data are available, there were an estimated 14.5 million visits to physicians made by adolescents for acne treatment.

Adolescent acne correlates best with pubertal stage, although lesions may become evident before secondary sexual characteristics appear. Early in puberty, blackheads and whiteheads predominate, and the midface (midforehead, nose, and chin) typically is involved. Later, inflammatory lesions become more prevalent, and the lateral cheeks, lower jaw, back, and chest are affected.

## Pathogenesis

Acne is a disorder of the pilosebaceous unit, comprised of a follicle or pore, sebaceous gland, and rudimentary or vellus hair. These specialized follicles are concentrated on the face, chest, and back, which explains why acne occurs in these areas. Although the pathogenesis of acne has not been defined, clearly multiple factors contribute (Fig. 1). Designing appropriate treatment requires an understanding of these factors.

## Hormones and Sebum Production

Androgens play an integral role in causing acne. At age 8 or 9 years, prior to the appearance of secondary sexual characteristics, adrenarche results in increased adrenal production of dehydroepiandrosterone sulfate (DHEAS). Rising levels of DHEAS, perhaps after conversion to more potent androgens such as testosterone and dihydrotestosterone, cause sebaceous glands to enlarge and produce more sebum. Sebum secretion peaks during adolescence and declines after age 20 years. In general, acne severity correlates with the rate of sebum secretion. Of note, sebum from patients who have acne is deficient in linoleic acid, a factor that may alter the keratinization process and contribute to follicular obstruction.

Despite the importance of androgens in causing acne, most males have normal hormone levels. For females, the picture is more complex: Hormone levels usually are normal, but free testosterone and DHEAS concentrations may be elevated, and sex hormone-binding globulin (SHBG) may be reduced.

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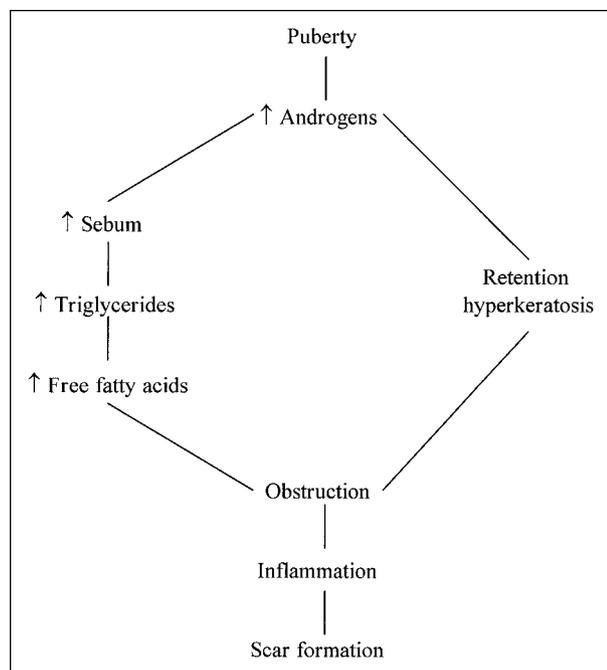


Figure 1. Pathogenesis of acne.

### Bacteria

*Propionibacterium acnes* is an anaerobic, gram-positive diphtheroid that colonizes pilosebaceous follicles following increases in sebum production. Although *P acnes* is a normal inhabitant of the skin, its numbers are higher in patients who have acne than in those who are unaffected. *P acnes* produces chemoattractant factors that cause polymorphonuclear neutrophils (PMNs) to enter pilosebaceous follicles. As PMNs ingest *P acnes*, hydrolytic enzymes are released that damage the follicle wall. Follicular contents then enter the surrounding tissue, where they incite inflammatory reactions that are manifested clinically as erythematous papules, pustules, or nodules. *P acnes* also produces lipases that hydrolyze triglycerides to free fatty acids (FFA), a factor that may contribute to the inflammatory process and follicular obstruction.

### Abnormal Keratinization

In acne, epithelial cells lining the follicle are not shed properly and become more cohesive. The result is a collection of cells and sebum that accumulates within the follicle. Termed “comedogenesis,” this process is central to the development of acne lesions. Although the trigger for comedogenesis has not been identified, proliferation or adhesion of keratinocytes, cytokine production, and the effects of androgens may be responsible.



Figure 2. Open comedones in the external ear and on the face. Reprinted from Krowchuk DP, Lucky AW. Managing adolescent acne. *Adolesc Med.* 2002;12:355–374 with permission of Hanley & Belfus.

### Genetics

Familial trends are well recognized in patients who have acne, but an exact pattern of inheritance has not been defined. Because the disease is common and modified by external factors, it is not possible to predict the severity of disease in an individual patient based on family history.

### Clinical Manifestations

The pathologic processes previously described have clinical correlates. Patients who have acne may exhibit obstructive or inflammatory lesions, scars, or cysts.

### Obstructive Lesions (Comedones)

Obstruction within the follicle initially is microscopic; such lesions are termed microcomedones. As comedones enlarge, they become apparent clinically as open comedones (blackheads) or closed comedones (whiteheads). Open comedones represent follicles that have widely dilated orifices (Fig. 2). The black color of these lesions does not represent dirt; rather, it may result from oxidation of melanin, interference with transmission of light



**Figure 3.** Closed comedones, small white papules without surrounding erythema, located on the forehead.

through compacted epithelial cells, or the presence of certain lipids in sebum. Closed comedones are small white papules that have no surrounding erythema (Fig. 3). They represent follicles that have become dilated with cellular and lipid debris but possess only a microscopic opening to the skin surface.

### Inflammatory Lesions

Inflammatory acne is characterized by erythematous papules, pustules, or nodules. Papules and pustules are small, measuring less than 5 mm in diameter (Fig. 4). Nodules measure more than 5 mm in diameter and often involve more than one follicle. As inflammatory lesions resolve, erythematous or hyperpigmented macules may remain for as long as 12 months; these often are mistaken for scars.

### Scars

Some patients who have acne develop scars as inflammatory lesions resolve. In general, scarring is most likely in patients who have large papules or nodules. On the face, acne scars appear as small pits; on the trunk, they usually are small hypopigmented spots. Rarely, patients develop hypertrophic or keloidal scars. Because scars may be irreversible, their presence should prompt the clinician to be aggressive in the selection of therapeutic agents active against the inflammatory component of the disease. True cysts, compressible nodules that lack overlying inflammation, also may be observed in patients who have acne.

### Evaluation

The first step in evaluation is to gather a history. Some helpful questions and their rationale are presented in Table 1. The physical examination should include the



**Figure 4.** Inflammatory papules and pustules located on the back of a patient who has severe acne. Reprinted from Krowchuk DP, Lucky AW. Managing adolescent acne. *Adolesc Med.* 2001;12:355–374 with permission of Hanley & Belfus.

skin of the face, chest, and back. Examination of other systems is dictated by findings from the history. To facilitate later comparison, a diagram of the face (Fig. 5) can be used to record the approximate number of inflammatory lesions and open and closed comedones. The clinician also can estimate the numbers and types of lesions present on the back and chest. This process can be accomplished quickly and provides an objective method of monitoring the patient's progress. In addition to this lesion count, it is helpful to make a global assessment of acne severity (eg, mild [Fig. 6], moderate [Fig. 7], or severe [Fig. 8]) that represents a synthesis of the number, size, and extent of lesions as well as the presence of scarring (Table 2).

### Differential Diagnosis

Conditions that may mimic adolescent acne are presented in Table 3.

Table 1. Key Elements of the Acne History\*

Question	Rationale
<b>For all patients</b>	
How long has the patient had acne? When did it begin? Which medications have been tried?	Early- or late-onset acne may indicate androgen excess. Which medications have been successful; which have not? Did treatment failures result from improper technique or insufficient duration of use? Did adverse effects occur?
Is the patient using other products to treat acne?	Many nonprescription acne preparations (eg, abrasive soaps) are irritating and may limit the patient's ability to tolerate more effective therapies.
Is the patient receiving other medications?	Topical or oral corticosteroids (including anabolic-androgenic steroids) may cause acne lesions. Lithium, isoniazid, hydantoin, and rifampin may worsen acne.
Does the patient use cosmetics or hair greases?	Cosmetics containing lanolin or oil or hair greases may cause or worsen acne.
Does the patient have recreational or occupational activities that may worsen acne?	Pressure applied by helmets, chin straps, shoulder pads, or tight occlusive garments may worsen acne. Oils or greases inadvertently applied to the skin as part of one's occupation can cause obstructive lesions.
Is there a history of other medical problems?	Adolescents who have a history of atopic dermatitis or those who report "sensitive" skin may not tolerate topical medications that dry or irritate skin.
<b>For females</b>	
Is the patient menstruating? Are there premenstrual flares? Is there a history of oligomenorrhea or hirsutism?	Premenstrual flares are common in women who have acne.  The presence of oligomenorrhea or hirsutism, coupled with the presence of acne, may suggest androgen excess caused by polycystic ovarian disease or late-onset congenital adrenal hyperplasia.
Is the patient sexually active?	Patients who are sexually active require effective contraception during treatment with isotretinoin.
Does the patient use hormonal contraception?	Certain hormonal contraceptives may worsen acne (see text). Women using oral contraceptives may require a secondary form of contraception if oral antibiotics are being used to treat acne (see text).
*Adapted from Krowchuk DP, Lucky AW. Managing adolescent acne. <i>Adolesc Med.</i> 2001;12:355-374	

## Laboratory Findings

Laboratory evaluation (eg, measurement of free testosterone, DHEAS, 17-hydroxyprogesterone) should be reserved for females who have early- or late-onset acne, acne associated with other evidence of androgen excess (eg, irregular menses, hirsutism, alopecia, or clitoromegaly), or acne unresponsive to conventional therapy.

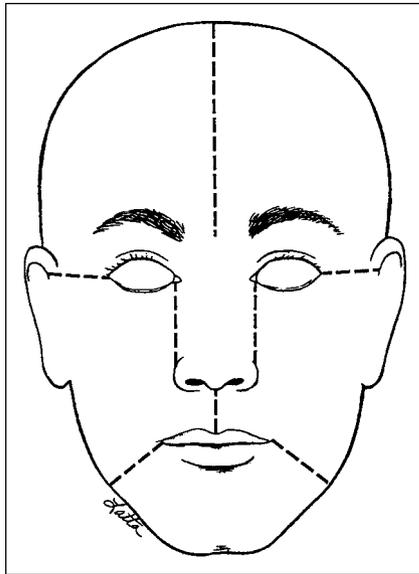
## Management

The successful management of acne depends on an understanding of the types of lesions present, the severity of disease, and the mechanism of action and possible adverse effects of available medications. Although there is no standardized treatment plan, rational guidelines exist (Table 4). Realistic goals of treatment are to reduce the number and severity of lesions and prevent scarring.

## Patient Education

The first step in management is to describe briefly the causes of acne and attempt to dispel commonly held myths:

- Acne is not caused by dirt, and frequent washing will not improve the condition. In fact, frequent washing or the use of harsh soaps may irritate the skin and limit a patient's tolerance for topical medications. To control oily skin, patients may be advised to wash once or twice daily using a mild nondrying soap or cleanser.
- For most adolescents, diet plays no role in acne. Occasionally, a patient may observe an apparent relationship between a particular food and a flare-up. In such instances, common sense dictates limiting the intake of this food.



**Figure 5.** In each region, the physician records the number of open comedones (OC), closed comedones (CC), and inflammatory lesions (IL). Redrawn with permission from Merck & Co. The original appeared in Lucky AW, et al. A multirater validation study to assess the reliability of acne lesion counting. *J Am Acad Dermatol.* 1966;35:559–565 and was used with permission of Elsevier Science.

The patient should be counseled about factors that may worsen acne. The information contained in Table I may help guide this discussion:

- Picking at, wearing athletic gear over, or otherwise traumatizing acne lesions may increase inflammation, prolong resolution of lesions, and increase the likelihood of scar formation.
- Cosmetics, sunscreens, and moisturizers, particularly those containing oils, may worsen acne. Advise the adolescent to select products that are labeled non-comedogenic or nonacnegenic.



**Figure 6.** Mild acne. A few small inflammatory lesions are present. Reprinted from Krowchuk DP, Lucky AW. Managing adolescent acne. *Adolesc Med.* 2001;12:355–374 with permission of Hanley & Belfus.



**Figure 7.** Moderate acne. Many inflammatory lesions are present. Reprinted from Krowchuk DP, Lucky AW. Managing adolescent acne. *Adolesc Med.* 2001;12:355–374 with permission of Hanley & Belfus.

- A variant of cosmetic acne, known as pomade acne (Fig. 9), may occur when greases used to style hair are applied inadvertently to the skin. Pomade acne occurs almost exclusively in African-Americans and is characterized by the presence of comedones located on the forehead and temporal areas. To prevent such lesions, patients can be advised to avoid placing hair care products on the skin.
- Young women often experience premenstrual exacerbations that may be caused by androgenic effects of progesterone, which is dominant during the second half of the menstrual cycle.
- Environmental factors may exacerbate acne among young people who come into contact with grease at work. Despite this, patients may be unwilling or unable to alter employment to accommodate concerns about acne.

Patients should be advised that acne treatment is a long-term process; often 6 to 8 weeks or longer are required to see improvement. Additionally, once lesions resolve, treatment may need to be continued until it is clear that new lesions are not appearing.

### Topical Therapies

Commonly employed topical preparations include benzoyl peroxide, antibiotics, retinoids, and salicylic acid.

**BENZOYL PEROXIDE.** Benzoyl peroxide (BP) primarily has an antibacterial effect and is useful in controlling



**Figure 8.** Severe acne. Numerous large inflammatory lesions and scarring are present. Reprinted from Krowchuk DP, Lucky AW. Managing adolescent acne. *Adolesc Med.* 2001;12:355–374 with permission of Hanley & Belfus.

inflammatory acne. It also may decrease the formation of FFA, thereby improving obstructive (comedonal) disease. These two actions make it an excellent drug in the management of patients who have mild inflammatory or mixed (eg, inflammatory and comedonal) acne. Because BP also prevents the emergence of antibiotic resistance among *P acnes*, it may be used adjunctively for patients receiving long-term oral or topical antibiotic therapy.

BP is available with or without a prescription in concentrations ranging from 2.5% to 10%. Over-the-counter products include creams, lotions, washes, and gels. Prescription forms generally employ a gel vehicle, a factor that enhances efficacy. A single daily application of a product containing a 5% concentration is adequate for most patients. Increasing the concentration to 10% does not enhance the therapeutic effect greatly, but does increase the likelihood of drying, erythema, and burning. BP usually is applied once daily, although twice-daily use may be beneficial for some patients.

As with all topical medications, BP is applied as a thin coat to all acne-prone areas rather than to individual lesions. When the entire face is to be treated, the patient may

be instructed to dispense an amount the size of a pea onto a finger tip. To distribute the medication, the finger is touched to each side of the forehead, each cheek, and the chin. The medication then is spread to cover the entire face, avoiding areas prone to irritation, such as the corners of the eyes, the alar folds, and the angles of the mouth. To treat larger areas, such as the back or chest, a BP wash applied during a bath or shower may be used, although greater efficacy may be achieved by applying the gel formulation and allowing it to remain in place for several hours (eg, overnight).

Adverse reactions associated with BP use include stinging after application and drying, redness, and peeling of the skin. These reactions may be prevented or limited by selecting an emollient or water-based gel, reducing the concentration of BP, or decreasing the frequency of application. Contact dermatitis is an unusual complication characterized by erythema, small papules, and pruritus. Patients should be advised that BP may bleach clothing and bedding. It is classified as pregnancy category C by the United States Food and Drug Administration (FDA), meaning that risk to the fetus cannot be ruled out.

**TOPICAL ANTIBIOTICS.** Topical antibiotics reduce concentrations of *P acnes*, inflammatory mediators, and possibly, FFA. As a result, these agents are most useful in treating mild-to-moderate inflammatory acne. The practical difficulties and cost associated with applying topical antibiotics to large areas limit their use to patients who have facial acne. In the United States, products containing clindamycin or erythromycin are available and have comparable efficacy. However, concerns about antibiotic resistance limit their use. Sodium sulfacetamide, with or without sulfur, also is available. Topical antibiotics are

**Table 2. Grading Scale for Severity of Facial Acne\***

Severity	Clinical Characteristics
Mild	—About one fourth of the face is involved —There are few to several papules or pustules, but no nodules or scarring
Moderate	—About one half of the face is involved —There are several to many papules or pustules and a few to several nodules. A few scars may be present
Severe	—Three quarters or more of the face is involved —There are many papules and pustules and many nodules. Scarring often is present

\*Adapted from Pochi PE, Shalita AR, Strauss JS, et al. Report of the consensus conference on acne classification. *J Am Acad Dermatol.* 1991;24:495–500 and Allen BS, Smith JG. Various parameters for grading acne vulgaris. *Arch Dermatol.* 1982;118:23–25.

Table 3. Some Conditions That May Mimic Adolescent Acne

Condition	Description	Differentiating Features
Adenoma sebaceum	Erythematous papules or nodules that appear in the nasolabial folds or on the cheeks of individuals who have tuberous sclerosis.	Lesions often appear during childhood (earlier than the lesions of acne); comedones are absent.
Acne rosacea	Erythematous papules, pustules, and scaling that involve the central face.	Typically occurs in adults; comedones are absent.
Gram-negative folliculitis	Sudden appearance of papules, pustules, and nodules in a patient being treated with oral antibiotics for acne.	Sudden worsening of acne in a patient who has been receiving long-term antibiotic treatment for acne vulgaris.
Keratosis pilaris	Small, rough-feeling, skin-colored or erythematous papules centered about follicles. A keratin plug emerging from the follicular orifice can be observed or palpated.	The presence of a central keratin plug differentiates keratosis pilaris from acne. Lesions also may be located on the upper outer arms, thighs, or buttocks.
Pityrosporum folliculitis	Erythematous papules and pustules that occur on the chest, shoulders, and upper back.	Lesions spare the face; a potassium hydroxide preparation performed on a pustule roof demonstrates budding yeast.
Steroid acne	Dome-shaped erythematous papules appearing on the face and trunk weeks after systemic corticosteroids have been begun.	Lesions have a monomorphous appearance (eg, only papules without comedones). There is a temporal relationship between the onset or worsening of acne and corticosteroid therapy.
Steroid rosacea	Erythematous papules or pustules that appear around the mouth and eyes. Often occurs in individuals who have applied potent topical corticosteroids to the face or have used inhaled corticosteroids.	Lesions are concentrated around the mouth (or eyes), and comedones are absent.

available in a variety of vehicles. As with other topical agents, lotions and creams are less drying than solutions or gels.

Products that combine agents enhance the therapeutic effect. For example, combinations of BP 5% and clindamycin or erythromycin are more effective than either drug alone. Beyond this, the inclusion of BP also prevents the development of antibiotic resistance. The primary disadvantage of combination preparations is the significantly greater cost. If cost is an issue, some clinicians provide separate prescriptions for the generic forms of BP and clindamycin and advise patients to apply the medications simultaneously.

An area of concern related to the use of topical or systemic antibiotics is the emergence of resistant forms of *P. acnes*. Between 1991 and 1996, the percent of patients attending a dermatology clinic in the United Kingdom carrying antibiotic-resistant organisms rose from 34.5% to 60%. In 1996, 47%, 41%, and 26% of these patients harbored strains of *P. acnes* that were resistant to erythromycin, clindamycin, or tetracycline, respectively. The majority of strains resistant to erythromycin exhibited cross-resistance to clindamycin and other macrolide antibiotics. Multiple drug resistance was observed in 18% of

isolates. Among propionibacteria resistant to tetracyclines, the degree of resistance to tetracycline is greater than that to doxycycline, which exceeds that to minocycline. An association between carriage of erythromycin-resistant propionibacteria and poor clinical response to oral treatment with this agent has been demonstrated. With this issue in mind, some clinicians do not prescribe oral erythromycin for acne or they use it only for previously untreated patients who are unlikely to harbor resistant organisms. Similarly, the use of topical erythromycin or clindamycin as monotherapy (ie, not combined with benzoyl peroxide) may be ineffective due to bacterial resistance.

**TOPICAL RETINOIDS.** Patients who have numerous blackheads and whiteheads will benefit from a topical retinoid. These agents normalize the keratinization process within follicles and reduce obstruction and the risk for follicular rupture. Tretinoin is the best known topical retinoid and is available in creams (0.025%, 0.05%, 0.1%), gels (0.01%, 0.025%), and a liquid (0.05%). The vehicle affects efficacy; creams are less potent than gels, which are less potent than the liquid. Newer formulations appear to be as effective but less irritating than

Table 4. Management Options for Facial Acne

Acne Severity	Lesion Type	Initial Treatment	If No Response
<b>Mild</b>	Comedonal	Benzoyl peroxide or topical retinoid <sup>1</sup>	If benzoyl peroxide is used initially, substitute with or add topical retinoid <sup>1</sup> once daily
	Inflammatory	Benzoyl peroxide (or topical combination preparation <sup>2</sup> )	Increase benzoyl peroxide application to twice daily or substitute combination product <sup>2</sup> or oral antibiotic <sup>3</sup>
	Mixed (ie, comedones and inflammatory lesions)	Benzoyl peroxide (or topical combination product <sup>2</sup> ) alone or with topical retinoid <sup>1</sup> (could substitute azelaic acid as monotherapy)	If benzoyl peroxide is used initially, add topical retinoid <sup>1</sup> once daily (for comedonal component) or substitute topical combination product <sup>2</sup> or oral antibiotic <sup>3</sup> (for inflammatory component)
<b>Moderate</b>	Comedonal	Topical retinoid <sup>1</sup>	Increase strength of topical retinoid <sup>1</sup>
	Inflammatory	Topical combination product <sup>2</sup> (or oral antibiotic <sup>3,4</sup> )	If topical combination product <sup>2</sup> is used, add or substitute an oral antibiotic <sup>3,4</sup> and add topical retinoid
<b>Severe</b>	Mixed (ie, comedones and inflammatory lesions)	Topical combination product <sup>2</sup> (or oral antibiotic <sup>3,4</sup> ) and topical retinoid <sup>1,5</sup> ; could substitute azelaic acid as monotherapy	Increase strength of topical retinoid <sup>1,5</sup> (for comedonal component); if combination product <sup>2</sup> is used alone, substitute oral antibiotic <sup>3,4</sup> (for inflammatory component) and add topical retinoid
	Comedonal	Topical retinoid <sup>1</sup> once daily	Increase strength of topical retinoid <sup>1</sup> or refer to dermatologist
	Inflammatory Mixed (ie, comedones and inflammatory lesions)	Oral antibiotic <sup>3,4</sup> and topical retinoid <sup>1,5</sup> Oral antibiotic <sup>3,4</sup> and topical retinoid <sup>1</sup>	Consider alternate antibiotic <sup>3,4</sup> or refer to dermatologist Consider increasing strength of topical retinoid <sup>1</sup> (for comedonal component) or alternate antibiotic <sup>3,4</sup> (for inflammatory component) or refer to dermatologist

<sup>1</sup>For example, tretinoin cream 0.025%<sup>2</sup>For example, clindamycin or erythromycin combined with benzoyl peroxide (clindamycin and erythromycin used alone are not favored due to potential antibiotic resistance)<sup>3</sup>For example, tetracycline (or possibly erythromycin) 250 to 500 mg twice daily<sup>4</sup>Some experts advise the use of benzoyl peroxide for patients treated with oral antibiotics to prevent the emergence of antibiotic-resistant *P. acnes*<sup>5</sup>Even in the absence of clinically apparent blackheads and whiteheads, most experts advise the use of a topical retinoid in conjunction with an oral antibiotic for patients who have moderate or severe inflammatory acne



**Figure 9.** Pomade acne, characterized by multiple closed comedones on the forehead

traditional varieties. Tretinoin also is available in generic form.

Adolescents who use tretinoin often experience irritation, redness, or dryness. For persons of color, this inflammation may result in hypo- or hyperpigmentation that can persist for months. To prevent or limit adverse effects, therapy often is begun with a low-strength preparation (eg, tretinoin cream 0.025%). Patients should be advised to dispense a small amount (a pea-sized dab is sufficient to cover the entire face) and to apply the medication every third night, progressing as tolerated over 2 to 3 weeks to nightly application. Tretinoin may cause an apparent temporary worsening of acne 2 to 3 weeks after treatment has begun and increased sensitivity to sunlight likely caused by skin irritation.

Because tretinoin is nearly identical in chemical structure to isotretinoin, some have raised concern about potential teratogenicity. However, there have been no reports of malformations occurring in infants born to women who used tretinoin during pregnancy. Nevertheless, tretinoin is classified as pregnancy category C, and for this reason, its use is avoided during pregnancy. Because BP inactivates tretinoin, the two drugs should not be applied simultaneously. Rather, BP may be applied in the morning and tretinoin at night.

Other retinoids also are available. Adapalene in a 0.1% gel formulation has been shown to be as effective as tretinoin gel 0.025% but less irritating. It is available as a 0.1% alcohol-free gel, cream, and solution or as pledgets. The principles of use and potential adverse effects are analogous to those of tretinoin. Like tretinoin, it is classified as pregnancy category C. Tazarotene is formulated in 0.05% and 0.1% gels and creams. Although proven effective in clinical studies, it is much more expensive and may be more irritating than other retinoids, and due to concerns about teratogenicity, it is contrain-

dicated in pregnancy. For these reasons, it is not prescribed widely for the treatment of acne.

**SALICYLIC ACID.** Salicylic acid reduces the formation of obstructive lesions; it is less effective than topical retinoids but less irritating. It is useful in the management of obstructive acne involving the face for patients who cannot tolerate retinoids or in the treatment of comedones on the trunk (where it may be impractical and too costly to apply a retinoid).

**AZELAIC ACID.** Azelaic acid 20% is both antibacterial and anticomedonal. It is applied twice daily and appears to be well tolerated, although some patients experience pruritus, burning, stinging, tingling, or erythema. No systemic toxicity has been reported. In one controlled trial, azelaic acid was as effective as BP 5%, tretinoin 0.05%, or erythromycin 2%. It is an alternative for patients who have mild-to-moderate inflammatory and comedonal acne or for those who have obstructive lesions who cannot tolerate tretinoin.

### Systemic Therapies

**ORAL ANTIBIOTICS.** Oral antibiotics possess greater efficacy than topical preparations; thus, they are prescribed for patients who have moderate-to-severe acne or inflammatory disease involving the trunk as well as the face. They exert their anti-inflammatory effect by decreasing bacterial colonization and inhibiting neutrophil chemotaxis; they also reduce the concentration of FFA in sebum.

Tetracycline and erythromycin are the oral antibiotics prescribed most often for the treatment of acne; both have been proven effective and are inexpensive. However, as discussed previously, bacterial resistance to erythromycin may limit its usefulness. Depending on disease severity and the patient's weight, each is initiated at a dose of 250 to 500 mg twice daily, although the higher dose usually is favored. Both are available in liquid form for patients who cannot swallow pills or capsules. Tetracycline may cause gastrointestinal disturbances. To assure absorption, it should not be taken with milk or other dairy products and should be taken on an empty stomach (eg, 30 min before or 2 h after a meal). Tetracycline should not be used during pregnancy or for patients younger than 9 years of age due to potential discoloration of teeth. Because tetracycline occasionally has caused esophageal ulceration, patients should be advised to take the medication with a large glass of water and to avoid reclining immediately after ingesting a dose. Other adverse effects include photosensitivity, vulvovaginal

candidiasis, and uncommonly, pseudotumor cerebri, hyperpigmentation, and onycholysis. The primary adverse effect of erythromycin is gastrointestinal upset that may be avoided by taking the medication with food.

For those who fail to respond to or cannot tolerate tetracycline or erythromycin, doxycycline often is effective. It is begun at a dose of 50 to 100 mg twice daily and can be taken with food. Unfortunately, doxycycline is even more likely than tetracycline to induce photosensitivity reactions. An alternative to doxycycline is minocycline, which is considered highly effective, particularly when *P. acnes* resistance is suspected. Minocycline is initiated at a dose of 50 to 100 mg bid; the latter dose is recommended when patients are suspected of harboring tetracycline-resistant propionibacteria. It is more expensive than other antibiotics and has uncommon but significant adverse effects, including pigmentation of the skin, teeth, or mucosa or autoimmune syndromes (eg, a serum sickness-like reaction, a hypersensitivity syndrome, lupus erythematosus-like reaction, and hepatitis). Several other oral antibiotics have been used in the treatment of acne but have not been studied well, including ampicillin, amoxicillin, cephalexin, and trimethoprim-sulfamethoxazole.

As with other acne therapies, 6 to 8 weeks often are required before oral antibiotics produce a significant clinical effect. Once the appearance of new lesions has ceased or been reduced satisfactorily, the dose may be tapered gradually or withdrawn.

Concern often is raised that oral antibiotics may diminish oral contraceptive efficacy by decreasing enterohepatic recirculation of contraceptive steroids, enhancing their hepatic degradation, or increasing their renal or fecal excretion. Research fails to support a systematic interaction between antibiotics used to treat acne (eg, tetracyclines or ampicillin) and oral contraceptives. However, it is possible that occasional oral contraceptive users experience declines in plasma ethinyl estradiol and progesterin concentrations during antibiotic treatment that could reduce contraceptive efficacy. Although this risk is very low, the Council on Scientific Affairs of the American Medical Association concluded that the use of an additional nonhormonal method of contraception or alternate contraceptive method be considered for women receiving long-term antibiotic therapy, particularly if they experience diarrhea or breakthrough bleeding. Clinicians should counsel patients about this concern, although the issue may be moot for adolescents because those using hormonal contraception are advised routinely to use a condom during all sexual encounters to protect against sexually transmitted infections.

**ISOTRETINOIN.** Isotretinoin is an oral analog of vitamin A that is highly effective for the treatment of severe recalcitrant acne. Despite its efficacy, oral isotretinoin therapy may be associated with important adverse reactions, the most serious of which is teratogenicity. For this reason, the drug should be prescribed only by physicians who have experience in its use. Presently, all isotretinoin prescriptions require that a qualification sticker be affixed. To obtain these stickers, physicians must have read educational materials provided by the manufacturer and signed a letter of understanding regarding isotretinoin use and its potential adverse effects on a fetus. Informed consent is required of all patients for whom isotretinoin is being prescribed.

Reports to the FDA have raised concern that isotretinoin use, through mechanisms unknown, may predispose patients to the development of depression or suicide. Although an association has not been demonstrated, clinicians caring for patients who are receiving isotretinoin should remain alert to the presence or development of mental health disorders, including depression and suicidal ideation.

**HORMONAL THERAPY.** Combined oral hormonal contraceptives (OCs), those containing an estrogen and progestin, may improve acne. Estrogen increases SHBG that, in turn, decreases biologically active free testosterone. OCs also suppress gonadotropin secretion, thereby reducing ovarian androgen production. Recent placebo-controlled trials document that OCs containing ethinyl estradiol (35 mcg) and the progestin norgestimate or ethinyl estradiol (20 mcg) and levonorgestrel improve acne. It is likely, however, that other OCs also have a beneficial impact on acne. Despite this, these agents are not viewed as primary therapy for acne but as an adjunct to standard medications.

Acne may be exacerbated by endocrine disorders such as polycystic ovarian syndrome or the metabolic syndrome (ie, insulin resistance, obesity, hypertension, and dyslipidemia). Use of long-acting progestin implants or depot medroxyprogesterone acetate may be associated with worsening acne.

### Complementary and Alternative Therapies

A number of complementary and alternative therapies have been advocated for the treatment of acne, but efficacy and safety have not been established for most. One agent that has received attention is tea tree oil, a mixture of terpenes and related alcohols that has antibiotic and antifungal properties. In a single-blind trial of 124 patients who had mild-to-moderate acne, a 5%

water-based gel formulation of tea tree oil was as effective as BP 5% water-based lotion. Although considered safe when used topically, it may cause contact dermatitis and, if applied undiluted, may induce comedogenesis. In young children, inadvertent ingestion of small amounts of tea tree oil has produced confusion, ataxia, and drowsiness.

Guggul (derived from the resin of the tree *Commiphora mukul*) was compared with tetracycline in patients who had inflammatory acne. After 3 months of therapy, patients in both groups experienced similar reductions in the numbers of lesions.

Therapies that have been employed and that are believed to be safe (but of unproven efficacy) include aloe vera (for acne scars), witch hazel (used as an astringent), calendula (marigold) tea (used as a compress), and lemon juice or cider vinegar (used as a face wash).

### Synthesis

Deciding which medication(s) should be prescribed for an adolescent who has acne is based on a synthesis of several factors, including the types and numbers of lesions present, the clinician's impression of the severity of disease, the extent of acne, the patient's experiences with medications, and personal preferences. Information contained in Table 4 is designed to help develop treatment plans. Beyond this, however, there is an art to treating acne, and two clinicians may differ in their approach to the same patient. Therapeutic choices also may be governed by formulary restrictions. In some states, for example, prescription topical acne medications are not approved for Medicaid reimbursement.

### Follow-up

A return visit typically is scheduled for 2 months after therapy has been initiated. However, patients should be encouraged to contact the office sooner with questions

or concerns regarding the use of their medications or possible adverse effects. At the follow-up visit, the clinician can assess compliance, determine the patient's impression of response to treatment, note the occurrence of adverse effects, and assess the effect of therapy. Using this information, the clinician can maintain or revise the therapeutic plan.

### Summary

Acne is the most common dermatologic disorder affecting adolescents. Although acne has no cure, clinicians can offer therapy that may limit the emotional consequences of the disease and prevent or reduce the likelihood of physical scarring.

### Suggested Reading

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## PIR Quiz

Quiz also available online at [www.pedsinreview.org](http://www.pedsinreview.org).

13. You are evaluating a 13-year-old boy who has numerous open and closed comedones involving the forehead, cheeks, and chin. There are no lesions on the chest or back. Of the following, the *most* appropriate treatment is:
  - A. Benzoyl peroxide topically.
  - B. Benzoyl peroxide/clindamycin topically.
  - C. Erythromycin topically.
  - D. Tetracycline orally.
  - E. Tretinoin topically.
14. A 16-year-old girl who has mild facial comedonal and inflammatory acne treated effectively with benzoyl peroxide 5% and tretinoin cream 0.025% presents with concern about an increase in acne lesions. Examination reveals approximately 20 inflammatory papules and pustules on her face and similar numbers of these lesions on her chest and back. There are rare comedones on the forehead. Of the following, the *most* appropriate next step in this patient's management is to:
  - A. Increase the potency of the topical retinoid.
  - B. Initiate an oral contraceptive.
  - C. Initiate isotretinoin orally.
  - D. Initiate tetracycline orally.
  - E. Substitute benzoyl peroxide/clindamycin topically for benzoyl peroxide.
15. You are counseling a 15-year-old girl about routine skin care for her acne and factors that may worsen the disease. Of the following, the statement that you are *most* likely to include in your discussion is that:
  - A. Eating fried foods will make acne worse.
  - B. The application of oil-based moisturizers may induce acne lesions.
  - C. The menstrual cycle does not affect disease severity.
  - D. The use of an abrasive soap will be beneficial.
  - E. Washing the skin frequently will prevent the appearance of acne lesions.
16. A *true* statement about acne is that:
  - A. Adolescent acne correlates best with chronologic age.
  - B. Early in puberty, acne is characterized by inflammatory lesions.
  - C. Genetic influences are unimportant in acne.
  - D. *P. acnes* primarily is responsible for causing follicular obstruction.
  - E. The severity of acne correlates with sebum secretion.
17. An 8-year-old boy who has refractory seizures and severe developmental delay is brought to you for treatment of acne. In his nasolabial folds and on his cheeks are erythematous papules. There are no blackheads or whiteheads. Of the following, the *most* likely diagnosis is:
  - A. Acne vulgaris.
  - B. Adenoma sebaceum.
  - C. Keratosis pilaris.
  - D. *Pityrosporum* folliculitis.
  - E. Steroid acne.

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*Pediatrics in Review* 2005;26;250

DOI: 10.1542/pir.26-7-250

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