

# Management of Acne Vulgaris

Supriya Ramanathan, MD; Adelaide A. Hebert, MD

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## Abstract and Introduction

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### Introduction

Acne is a chronic and multifactorial skin condition affecting about 80% of persons aged 11 to 30 years, the majority of whom are adolescents (Morelli, 2007, Shamban and Narurkar, 2009, Zaenglein and Thiboutot, 2006). Although acne has no cure and has the potential to cause emotional distress and permanent scarring, proper treatment can control the disease and greatly limit the morbidity. In recent years, acne treatment guidelines have been revised based on a better understanding of acne pathophysiology, and they currently aim to target as many pathogenetic factors as possible. This practice guideline will highlight the most recent treatment guidelines for adolescent acne.

### Etiology

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Acne lesions occur in the pilosebaceous unit, which is made up of the hair follicle, the hair shaft, and the sebaceous gland. The initiating step in all acne lesions is the formation of the microcomedone. With the onset of puberty, the level of androgens increases, which causes enlargement of the sebaceous glands and increased sebum production. Simultaneously, an increased shedding of keratinocytes into the lumen begins, instead of the normal shedding of one keratinocyte at a time for excretion. This aggregate of cells and sebum forms the microcomedone.

*Propionibacterium acnes* is a normal inhabitant of skin that colonizes the pilosebaceous follicle. In persons prone to acne, the inflammatory response to *P. acnes* results in damage to the follicle and release of follicular contents into the surrounding tissue, where they induce further inflammatory reaction, resulting in erythematous papules, pustules, and nodules.

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Thus the four factors involved in acne are increased sebum production, abnormal desquamation of keratinocytes, the presence of *P. acnes*, and inflammation. The relative contribution of each factor determines the type of lesion (Morelli, 2007, Zaenglein and Thiboutot, 2006).

When the initial microcomedone enlarges, it becomes either an open comedone with a widely dilated orifice (blackhead) or a closed comedone (whitehead). The black color reflects not an absence of hygiene but the oxidation of melanin within the open orifice. This condition is comedonal acne.

Inflammatory acne is characterized by erythematous papules, pustules (less than 5 mm in diameter) and nodules (more than 5 mm in diameter). Postinflammatory hyperpigmentation, which often is mistaken for scars, can last as long as a year. Irreversible scars can occur following resolution of lesions and appear as pits or hypopigmented spots.

Early in puberty, comedonal acne predominates, typically affecting the forehead, nose, and chin. Later in puberty, inflammatory lesions also are seen, affecting the cheeks, jaw, back, and chest.

### Consensus Guidelines

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Consensus guidelines have been developed by international committees and are based on expert opinions as well as evidence-based medicine (Strauss et al., 2007, Thiboutot and Gollnick, 2009, Zaenglein and Thiboutot, 2006). These guidelines propose new management protocols for acne.

The main change from previously published algorithms is the recommendation that topical retinoids should be the first line of treatment, either alone (when comedones predominate) or in combination with an antimicrobial agent (when inflammatory features predominate). Topical retinoids have become the mainstay of maintenance therapy as well.

## History

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According to Krowchuk (2005), the following elements are key in developing an accurate acne history:

- Duration of acne
- Previous medications tried (especially the technique and duration of use, which might have affected efficacy)
- Other acne-provoking products currently being used (e.g., medications, cosmetics, and hair grease)
- Activities that might be contributing to acne (e.g., use of occlusive garments and chin straps)
- Medical history/review of systems, including the following topics:
  - Eczema (an indication that the patient might not tolerate "drying" topical medications)
  - Symptoms related to menses, such as premenstrual flares
  - Oligomenorrhea and hirsutism (which, along with acne, suggests polycystic ovary syndrome)
  - Sexually active female patient (hormonal contraception, depending on the type, usually diminishes the occurrence and severity of acne)

## Physical Examination

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- Type and severity of acne
  - Mild acne involves less than one fourth of the face and includes the presence of papules and pustules but no nodules or scarring
  - Moderate acne includes about half of the face with some nodules and few scars
  - Severe acne involves three quarters or more of the face and includes many nodules and scars
- Signs of androgen excess (e.g., hirsutism, alopecia, premature adrenarche or body odor, and accelerated growth)

## Laboratory Tests

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- Routine testing is not recommended unless androgen excess is a concern
  - Ascertaining levels of total and free testosterone, dehydroepiandrosterone, dehydroepiandrosterone sulfate, prolactin, luteinizing hormone, follicle-stimulating hormone, and thyroid-stimulating hormone, as well as obtaining a hand film for bone age in prepubertal patients, may be helpful to screen patients for whom polycystic ovary syndrome is suspected (Antonίου, Dessinioti, Stratigos, & Katsambas, 2009)

## Treatment

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### Topical Treatments

Topical treatment choices include topical retinoids (e.g., tretinoin, adapalene, and tazarotene), benzoyl peroxide (BPO), combinations of BPO and topical antibiotics (e.g., erythromycin and clindamycin), combinations of retinoids and antibiotics (e.g., clindamycin and tretinoin), combinations of benzoyl peroxides and retinoids (adapalene), salicylic acid, and azelaic acid (Thiboutot and Gollnick, 2009, Zaenglein and Thiboutot, 2006).

### Topical retinoids

- Topical tretinoin has direct anti-inflammatory properties as well as the ability to regulate keratinocyte desquamation. Therapy can prevent microcomedone formation, reduce the number of existing lesions, and decrease formation of new lesions; benefits are seen with inflammatory and non-inflammatory lesions. Thus topical tretinoin has become the mainstay of treatment as well as maintenance.
- Topical tretinoin is available as creams (0.025%, 0.05%, and 0.1%), which are less potent than gels (0.01%, 0.025%).
- Treatment with tretinoin should begin at the onset of acne for best results, and it should be applied to the entire affected area. Spot treatment does not address the underlying pathophysiology of acne.
- Several suggestions can be made to patients to increase tolerance and compliance. Treatment should begin with a lower strength or a less irritating formulation (e.g., 0.025% cream) or a reduced frequency of application (every second or third day). Suggest washing off the medication after a period of contact, and emphasize that a pea-sized dab divided into the four quadrants is sufficient for the entire face. Remind the patient that retinoids are not a spot treatment and that he or she should discontinue the use of concomitant scrubs and other over-the-counter (OTC) products.
- Burning, redness, dryness, and increased sensitivity to sunlight can occur. Enhanced sensitivity to the sun can be controlled through the use of a sunscreen. Retinoid-induced dermatitis can be lessened with the application of an OTC cream or lotion that contains ceramides.
- Retinoid activity in some topical formulations is inactivated by BPO, which must be washed off prior to application of a retinoid. Hence BPO usually is applied in the morning and a retinoid is applied at night. This regimen also helps reduce the likelihood of photosensitivity.
- Adapalene is the best-tolerated retinoid. It is designed specifically to penetrate the pilosebaceous unit. Adapalene is photostable and is resistant to inactivation by BPO. It is available as a 0.1% and 0.3% gel, a 0.1% cream, and a 0.1% solution, and it is believed to be as effective as tretinoin 0.025%.
- Tazarotene (available as a 0.05% or 0.1% gel or cream) also is effective but is more expensive, may be more irritating than other retinoids, and is contraindicated in women who are pregnant.

### Benzoyl Peroxide

- BPO is a potent antimicrobial agent and can significantly improve anti-inflammatory acne. *P. acnes* and other microorganisms have not, to date, developed resistance to BPO.
- BPO concentrations range from 1% to 10% in various formulations including soaps, washes, creams, gels, and lotions. The 5% formulation generally is well-tolerated with the least adverse effects.
- BPO formulations are available OTC in a wide variety of alcohol- or water-based products. Water-based products are useful for persons with dry or sensitive skin; alcohol-based products are preferred for persons with oily skin because they are more drying. Prescription formulations generally utilize a gel vehicle, which are more efficacious than the OTC formulations because of the penetration into the follicle, where the pathophysiology of acne takes place.

- The most common adverse effect of BPO is skin irritation but this effect generally improves over time. Starting BPO at a lower concentration in persons with sensitive skin is helpful. A pea-sized amount of product is sufficient for the entire face. Using a BPO wash in the shower is beneficial when lesions are widely distributed on the chest and back. The wash-on products must be left on the skin for 20 to 30 seconds to allow penetration into the follicle. These products then may be rinsed off the skin.
- Patients should be cautioned of the possibility that BPO may bleach fabrics and bedclothes.

### **Topical Antibiotics (Erythromycin and Clindamycin)**

- Topical antibiotics inhibit the growth of *P. acnes*. They are effective in mild inflammatory acne and are well-tolerated. Resistance is common; these products are no longer recommended as monotherapy.

### **Combination Therapy**

- For patients with comedonal and inflammatory acne, combination therapy using a topical retinoid with either an antibiotic (topical or oral) or BPO or an antibiotic/BPO combination provides synergy and faster clearing. To reduce the incidence of bacterial resistance, the oral antibiotic typically is discontinued after three months. Combination products of antibiotic and BPO have not lead to bacterial resistance, even when used over long periods.

### **Salicylic Acid**

- Generally, salicylic acid is considered less effective than topical retinoids but also is less irritating. This anti-inflammatory agent is useful in patients who do not tolerate retinoids or in the treatment of comedones on the trunk, where it may be expensive to use a retinoid. Patients in the very early stages of acne with a few comedones benefit from washes that contain 2% salicylic acid.

### **Azelaic Acid**

- An azelaic acid 20% cream formulation has keratolytic and anti-inflammatory properties and is a useful alternative for patients with mild to moderate acne or those who cannot tolerate tretinoin.

### **Dapsone**

- Dapsone is available as a 5% gel. This topical formulation should be applied to the entire face twice a day to control acne.

## **Systemic Treatment**

### **Oral Antibiotics**

The following general guidelines pertain to use of oral antibiotics:

- Use in patients with moderate to severe inflammatory acne
- Avoid monotherapy
- Use BPO to reduce resistance or combine with a topical retinoid
- Use for at least six to eight weeks for visible improvement; remind patients that this therapy takes time and that results will not be seen overnight
- Re-evaluate the need for an oral antibiotic at 12 to 18 weeks

- Note: The doses listed below and in the table are those reported for adolescents; the patient's weight should always be considered when prescribing medications

### **Tetracycline**

- Tetracycline has been used more often than any other oral antibiotic to treat acne
- Tetracycline is inexpensive and well-tolerated
- The starting dose is 500 to 1000 mg/day and gradually decreased after six to eight weeks to the lowest dose that maintains clear skin
- Tetracycline should be taken one hour before or two hours after meals to facilitate absorption
- Tetracycline cannot be used for persons younger than nine years, those who are pregnant or breast feeding, and patients should be cautioned about photosensitivity

### **Doxycycline**

- Doxycycline is used at doses of 50 to 100 mg twice daily as an alternative to tetracycline
- Doxycycline can be taken with food and a full glass of water to lessen gastrointestinal distress, but it is more likely to induce photosensitivity reactions

### **Other Systemic Antibiotics**

- The following alternative antibiotics also may be prescribed:
  - Erythromycin (widespread resistance)
  - Minocycline (uncommon but significant adverse effect profile)
  - Lime cycline (for use outside the United States)
  - A combination of trimethoprim, 160 mg, and sulfamethoxazole, 800 mg, as one tablet taken twice a day and trimethoprim, 300 mg twice daily, are alternatives in allergic patients or those who are unresponsive to other agents

### **Hormonal Therapy**

- Combination oral contraceptives are indicated in women for whom conventional therapy has failed or who have persistent inflammatory acne on the lower face and neck, hyperandrogenism, or additional reasons for its use, such as a need for contraception or menstrual regulation or who are about to begin taking isotretinoin (which, because it is teratogenic, mandates effective birth control).
- Spironolactone in dosages of 50 to 200 mg has been shown to be effective in treating acne but can cause hyperkalemia.
- Flutamide, a, nonsteroidal anti-androgen drug (which has the potential for hepatic failure) and oral corticosteroids (which are used in a short burst for highly inflammatory disease and in persons with proven adrenal hyperactivity) are other agents with some role in the hormonal management of acne.

### **Isotretinoin**

- Isotretinoin is indicated for persons with severe recalcitrant nodular acne or who have lesser degrees of acne that is treatment resistant or that produces physical or psychological scarring.
- Isotretinoin is a potent teratogen and is to be used in women of childbearing age only if they are participating in the approved pregnancy prevention and risk management program called iPledge ([www.ipledeprogram.com](http://www.ipledeprogram.com)). This program requires mandatory registration of all patients receiving this drug. Physicians who prescribe this medication also must be registered with the program.

- The dose is 1.0 to 2.0 mg/kg/day over a 20-week course. Initial flaring may be minimized by starting at lower than 0.5 mg/kg/day, and in severe cases, pretreatment with oral steroids may be considered.
- Isotretinoin has many adverse effects including cheilitis, conjunctivitis, hypertriglyceridemia, elevated serum cholesterol levels and liver enzymes, blood dyscrasias, dry eyes and mouth, photosensitivity, and pruritus. Blood counts, lipid levels, and liver enzymes should be monitored at baseline and monthly while the medication is taken and 1 month after therapy has been stopped. Pregnancy tests are required of women of childbearing potential 30 days before the initiation of therapy, at the time of initiation of therapy, each month while undergoing therapy, and 30 days after completing therapy. The results of each pregnancy test must be recorded on the iPledge Program Web site ([www.ipledgeprogram.com](http://www.ipledgeprogram.com)).

## Maintenance Therapy

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Once clinical improvement is achieved, a topical retinoid should be continued as part of maintenance because microcomedone formation begins immediately after discontinuation of a retinoid. Oral and topical antibiotic therapy should be discontinued immediately after inflammatory lesions are under good control. If continued antimicrobial therapy is needed, BPO can be used in conjunction with a topical retinoid.

## Miscellaneous Therapy

- Comedone removal can improve appearance, which is often helpful on a short-term basis, but it does not alter the course of the disease.
- Intralesional corticosteroid injections are effective in individual acne nodules.
- Physical modalities such as glycolic and salicylic acid peels can be of benefit.
- Newer laser and intense pulsed light treatments can help with acne control.
- Limited data suggest that complementary therapies are of benefit. These therapies include herbal agents such as tea tree oil (which may be effective topically but can cause contact dermatitis; oral ingestions can produce confusion and ataxia), guggul (which is derived from the resin of a tree and has benefits in treating inflammatory acne), aloe vera (which helps diminish acne scars), witch hazel (an astringent agent), calendula (marigold), tea (used as a compress) and lemon juice or cider vinegar (used as a face wash). Hypnosis and biofeedback may have some efficacy as well.

## Patient Education

- Patients should be instructed to wash skin with a mild, non-drying soap or cleanser. Frequent washing/scrubbing and use of harsh soaps should be discouraged.
- Patients should select hair and skin products, including cosmetics, sunscreens, and moisturizers, that are labeled non-comedogenic or non-acnegenic.
- Patients should avoid traumatizing acne lesions (for example, by picking or squeezing lesions and by using occlusive athletic gear over acne) to avoid scarring.
- Patients should be instructed that treatment is a long-term process requiring several weeks to months for the control of initial symptoms, followed by ongoing maintenance therapy.
- Patients should be warned of the potential for initial "worsening" because of dryness or irritation of the skin before the skin clears. They should be reminded to moisturize for dryness with a non-comedogenic moisturizer and to use a sun block.
- Maintenance therapy should be discussed, because acne tends to recur without an ongoing maintenance regimen. Patients should be reassured that one's diet, including soda and chocolate, does not aggravate acne.