Acne: A Review of Diagnosis and Treatment

Noah S. Scheinfeld, JD, MD

Educational Objectives

After reviewing this article, readers should be able to:

- Choose the most effective therapy for the non-inflammatory and inflammatory manifestations of acne.
- Describe the role that hormonal imbalance plays in the etiology of acne.
- Identify the mechanism of action of the topical and oral therapies for acne.

Abstract

Acne vulgaris (acne) is probably the most common dermatological complaint in the U.S. Acne has a range of presentations and manifestations, thus apparently comprising many disease states. Although acne is not an infectious disease, specimens of bacteria such as Propionibacterium acnes, Propionibacterium granulosum, and Staphylococcus epidermidis can be obtained for culture from the eruptions of acne. Other common associations of acne include hormonal imbalances and follicular hyperkeratinization.

Therapies for acne are varied. The most cost-effective treatment option is benzoyl peroxide; for comedonal acne, the most effective therapy consists of retinoids. Isotretinoin remains the most potent therapy. Other treatments include oral and topical antibiotics, topical sulfur agents, topical azelaic acid, and oral contraceptives.

Introduction

Acne vulgaris (acne) affects almost all humans at some point in their lives. Acne is the most common condition treated by American dermatologists. Approximately seven million new cases are diagnosed each year in the U.S.1-34 The cost of prescription and over-the-counter (OTC) medications exceeds $1 billion annually.

Acne engenders substantial psychosocial morbidity. A study from England notes that people with severe acne have a higher rate of unemployment than those with clearer skin.3 Other studies have indicated an adverse impact on social relationships. Teenagers with acne are at an increased risk of depression (odds ratio, 2.04), anxiety (odds ratio, 2.3), and suicide attempts (odds ratio, 1.83).10

Acne commonly affects people between adolescence and the end of life. It is more common in boys than in girls during puberty (ages 10 to 12).30 Between the ages of 21 and 45 years, acne is more common in women than in men of a similar age. In one community-based study from the United Kingdom, the estimated prevalence of facial acne was 14% in adult women between 26 and 44 years of age.24 By age 45 years, 5% of both men and women still experience a range of acne lesions; however, comedones are common in the elderly, even independent of solar elastosis.

In a study of hospitalized patients in geriatric wards, Kumar and Marks found a prevalence rate of 26% for senile comedones.33 Acne rarely occurs in prepubescent children as a result of an endocrinopathy; more commonly, it occurs in neonates as a transient eruption caused by circulating maternal hormones.

Stages of Acne

Morphologically, acne is divided into inflammatory and non-inflammatory subtypes that can overlap. Papules, pustules, and nodules characterize inflammatory lesions; comedones (open and closed) characterize non-inflammatory lesions.35 Acne is graded on a scale of mild, moderate, and severe, with intermediate grades and severe variants.35

- Mild acne can present simply with comedonal or mild papulopustular lesions, with or without the presence of a few papulopustules.
- Moderate acne presents with numerous comedones, few to numerous pustules, and few small nodules, without residual scarring.
- In severe acne, papulopustules are numerous, many nodules appear, inflammation is manifested, and scarring is present.
- Very severe acne is characterized by sinus tracts, grouped

Dr. Scheinfeld is Assistant Clinical Professor in the Department of Dermatology at Columbia University and a dermatologist in private practice. He can be reached at 30 Central Park South, Suite 2D, New York, New York 10019 (212-991-6490).
comedones, numerous deeply located nodules, and severe inflammation and scarring.

Mild or moderate non-inflammatory acne can be treated with topical retinoids. Non-inflammatory acne of a moderate-to-severe or greater grade is best treated with oral isotretinoin (Accutane, Roche).

Inflammatory acne of any grade can benefit from the use of topical benzoyl peroxide (e.g., Benzac, Galderm; Benzagel, Aventis). The initial treatment of mild inflammatory acne can be OTC benzoyl peroxide without the need for intervention by a medical doctor. Mild inflammatory acne that does not respond to benzoyl peroxide can benefit from a variety of topical treatments.

For moderate comedonal and mild-to-moderate papulopustular acne, combination therapy with either benzoyl peroxide or topical retinoids plus topical antibiotics such as erythromycin (e.g., Akne-Mycin, DPT Laboratories) or clindamycin phosphate (Cleocin T, Pfizer) has proved effective. Six to eight weeks should be allowed for most treatments to work before the regimen is altered.36

Moderate inflammatory acne is best treated with oral medications that include antibiotics, oral contraceptives for female patients, and isotretinoin for patients who have not responded to other oral medications.37,38

Clinical Presentation

As a polymorphic disease with non-inflammatory and inflammatory aspects, acne has a wide spectrum of chronic manifestations, including papules, pustules, open or closed comedones, and/or cysts. Most men and women with acne manifest a mixture of non-inflammatory and inflammatory lesions; however, some patients have predominantly one type of lesion or the other type.35

The lesions appear in characteristic locations and possess a typical appearance. Acne is most commonly manifested on the face, chest, and back; it can appear on the lower back as well. It usually spares the neck, the scalp, and the skin behind the ears.

Comedones are typically present only on the face, whereas papules and pustules of acne can appear on the face, chest, and back. Milia and cysts, although distinct from acneiform eruptions, commonly occur with these eruptions.

Common symptoms include pain, tenderness, and erythema in the areas where acne cysts and swollen skin are present. In particular, these cysts, if inflamed, can be painful. In some cases, acne appears to be related to excess sebum production and oily skin.

Differential Diagnosis

The differential diagnosis of acne includes gram-negative folliculitis, perioral dermatitis, sebaceous hyperplasia, syringoma, tuberous sclerosis (adenoma sebaceum), trichoepithelioma, Demodex folliculitis, bacterial folliculitis, and papular sarcoidosis. The diseases that most closely resemble acne, but are said to be distinguishable from it, include:

- **gram-negative folliculitis**: occurs after months of therapy with tetracycline (e.g., Sumycin, Par); responds only to sulfa antibiotics, such as sulfamethoxazole/trimethoprim (Bactrim, Women First) or isotretinoin; and is the type from which gram-negative pathogens can be obtained for culture.20
- **rosacea**: classically defined as a facial eruption lacking comedones
- **perioral dermatitis**: thought to be a variation of rosacea
- **acneiform drug eruptions**: most commonly associated with epidermal growth factor blockers but related, at a lower incidence, to lithium and phenytoin (Dilantin, Pfizer)
- **eosinophilic pustular folliculitis**: most closely associated with HIV infection in the U.S. but not uncommon in the Japanese population

Acne can occur in tandem with other eruptions and can result in scarring that lasts beyond its resolution. It can overlap with acne rosacea or seborrheic dermatitis.19 It can also be concurrent with gram-negative folliculitis; the latter may be manifested following months of therapy with antibiotics (typically tetracyclines). Acne can leave behind hypertropic scars, pitted (“icepick”) scars, sinus tracts, keloids, and atrophic scars.

In men of color, pseudofolliculitis is a common sequela of acne in the beard area. In old age, people who had acne in earlier life and experienced actinic damage can manifest Favre–Racouchot syndrome. The relationship of the syndrome to acne is unclear.

Biofilm and Enzymatic Tools of *P. acnes*

To understand the mechanisms, utility, and basis of the cornerstone of topical therapy—retinoids and benzoyl—it is important to comprehend the organism *P. acnes*.30

*P. acnes* resides within the pilosebaceous unit in a biofilm. An important factor in the persistence and effect of *P. acnes* is its ability to form such a biofilm, including the production of an exopolymer that is similar in appearance to the polysaccharide intercellular adhesin of *S. epidermidis*. This glycocalyx polymer forms a protective exoskeleton and may be an important immunogenic agent that feeds the inflammation that sometimes is associated with acne.8 This biofilm functions as a physical barrier that prevents the elevation of concentrations of antimicrobial agents proximate to the bacteria sufficient to hinder the bacteria.8 The role of biofilm probably explains the parameters of successful treatment of acne, including:

- the need for prolonged courses of oral antibiotics.
- the lack of consistent clinical relevance of the presence of *P. acnes* resistant to antibiotics to treatment with oral antibiotics.
- isotretinoin’s capacity to cure acne.
- the mechanisms that underlie the effectiveness of benzoyl peroxide, including its generation of free radicals, when it is placed on the skin.

*P. acnes* possesses other means of engendering acne. The organism can produce active enzymes and inflammatory
mediators that can contribute to acne’s progression, including smooth-muscle contracting substances, lipases, proteases, hyaluronate lyase, and phosphatase. Lipases can convert triglycerides in sebum to free fatty acids; this increases the clumping of P. acnes in the follicles, thereby facilitating an increase in the number of bacteria.

**Etiology**

Follicular hyperkeratinization underlies the development of comedones, the characteristic acne lesion. Although many patients believe that acne stems from a failure to clean the face effectively and sufficiently, researchers have noted it is a failure of the skin and the pores to slough off dead skin cells. Hyperkeratinization is related to the presence of P. acnes in the follicles as it unleashes its enzymatic armamentarium and hides behind the biofilm.

Comedones can be open (blackheads), or closed (whiteheads). Retinoids that normalize follicularization are the most effective therapy for acne. Preparations include topical retinoids such as tretinoin (all-trans retinoic acid) (e.g., Retin-A, Ortho) and oral retinoids such as isotretinoin (Accutane).

Acne also involves neutrophil pathology and inflammation. The pustules of acne are filled with neutrophils, which damage the follicle and which are associated with erythema. Because acne is characterized by neutrophils—the “foot soldiers” of inflammation—antibiotics that have anti-inflammatory activity may be used. Examples include tetracyclines, macrolides (e.g., Biaxin, Abbott), minocycline (Minocin, Wyeth), doxycycline (e.g., Vibramycin, Pfizer) at full and submicrobial doses, azithromycin (Zithromax, Pfizer), and erythromycin (e.g., Akne-Mycin).

Acne is related to hormonal imbalances. Androgen levels in patients with acne are higher than in controls; people with androgen insensitivity syndrome do not develop acne. Acne flares during a woman’s menstrual period, and it may also affect men who take anabolic steroids. It responds to the use of medications that work to “even out” hormonal levels, such as oral contraceptives (e.g., norgestimate/ethinyl estradiol [Ortho Tri-Cyclen, Ortho-McNeil]) or substances that block female hormones (e.g., spironolactone [Aldactone, Pfizer]).

As a hormonal disease, acne, particularly in women, is related to excess androgen and is strongly associated with polycystic ovary syndrome (PCOS). If patients have irregular menstrual periods and acne, an investigation is recommended to determine the cause of the excess androgen. Sex hormone-secreting tumors, congenital adrenal hyperplasia, and other endocrine diseases marked by excess androgen can result in acne. Men who take testosterone or anabolic steroid supplements also tend to develop acne.

A variety of miscellaneous mechanisms are associated with acne. On the cellular level, acne has been found to be related to defects in T-cell receptors. It is a disease of autoimmunity of sorts in which the body seems to respond to itself with inflammation. Some authors have linked an intake of fatty foods to the occurrence of acne, but this association remains controversial. Smoking may be a clinically important contributory factor to the prevalence and severity of acne.

Topical applications of a variety of substances have been linked to the development of acne. Chloracne, which may be considered to be an acniform eruption rather than a true manifestation of acne, can be associated with topical exposure to halogens or oils. Examples of halogens include bromides (present in cough syrups and asthma medications), chlorides, fluoride, and iodides (in salt or seafood). Women sometimes develop acne on areas of the face that are covered by hair as well as by oils or pomades for the hair. Mechanics tend to have acne because of the use of oils in their work.

Acne can also result from oral medications (Table 1). Lithium is a potent inducer of neutrophils and can cause and exacerbate acne. Epidermal growth factor blockers are linked to an acniform eruption, whose severity parallels clinical effect, which histologically is a folliculitis.

**Topical and oral preparations that induce or worsen acne include corticosteroids, which can cause steroid acne; this may be characterized by monomorphous dome-shaped papules on the chest. Steroid acne is often encountered in patients with collagen–vascular diseases or with neurological pathology that requires protracted courses of oral corticosteroids (in particular, potent ones such as dexamethasone).**

Acne excoriée (pathological or compulsive picking at the skin) commonly occurs in young women who pick at scattered acne papules, which are converted into scars; this is as much a psychological disease as a physical disease. Treatment involves selective serotonin reuptake inhibitors (SSRIs) to relieve the urge to pick and isotretinoin to erase all traces of acne that are exacerbated by picking.

---

**Table 1 Classes and Types of Medications That Can Cause Acne**

<table>
<thead>
<tr>
<th>Antipsychotic Agents</th>
<th>Hormones</th>
<th>Anticonvulsants</th>
<th>Antibiotics</th>
<th>Elemental Agents</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trazodone (Deseryl)</td>
<td>Estrogens</td>
<td>Phenytion</td>
<td>Isoniazid</td>
<td>Halogens</td>
<td>Imatinib mesylate (Gleevec)</td>
</tr>
<tr>
<td>Haloperidol (Haldol)</td>
<td>Anabolic-androgenic steroids</td>
<td>Lamotrigine (Lamictal)</td>
<td></td>
<td></td>
<td>Gefitinib (Iressa)</td>
</tr>
<tr>
<td>Lithium Aminoptine (Survector) (off-patent)</td>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Therapies for acne are varied and include proper cleaning regimens, topical agents, oral antibiotics, oral retinoids, and oral hormonal therapies. Available treatments are outlined in Table 2.

The skin of patients with acne can be easily irritated by topical agents that are used to treat the condition. The use of mild, non-drying cleaning products and non-comedogenic moisturizers may help reduce this irritation.

### Table 2: Therapies for Acne

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin 1% lotion, gel, sol, pad (Cleocin)</td>
<td>Azelaic acid 20% cream (Azelex); Azelaic acid 15% gel (Finacea)</td>
<td>Tetracycline 500 mg b.i.d. (Sumycin)</td>
<td>Tazarotene cream gel (Tazorac, Avage)</td>
<td>Oral contraceptives (Ortho Tri-Cyclen)</td>
<td>Nicotinamide 1.5 g q.d. divided in two or three doses (Nicomide)</td>
</tr>
<tr>
<td>Erythromycin ointment 2% (Akne-Mycin)</td>
<td>Sodium sulfacetamide 10%/sulfur 5% combination lotion, cream, pads, short contact preparation, cleanser (Novacet, Sulface)</td>
<td>Doxycycline 50–100 mg b.i.d. (Vibramycin)</td>
<td>Adapalene cream, gel (Differin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzoyl peroxide 5%/clindamycin 2% combination gel, pad (BenzaClin)</td>
<td>Sodium sulfacetamide 10% lotion</td>
<td>Minocycline 50–100 mg b.i.d. (Minocin)</td>
<td>Extended-release minocycline HCl (Solodyn) 45, 90, or 135 q.d.</td>
<td></td>
<td>Oral zinc gluconate 200 mg q.d.–b.i.d.</td>
</tr>
<tr>
<td>Benzoyl peroxide 5%/erythromycin 3% combination gel, pad (Benzamycin)</td>
<td>Benzoyl peroxide gel, wash q.d.–b.i.d. (Benzac, Benzagel)</td>
<td>Sulfamethoxazole/trimethoprim double-strength b.i.d. (Bactrim)</td>
<td>Tretinoin 0.025%/clindamycin phosphate 1% gel (Vela; not yet approved)</td>
<td></td>
<td>Ocimum gratissimum oil (basil) (topical)</td>
</tr>
<tr>
<td>Topical dapsone 5% gel (Aczone)</td>
<td>Azithromycin 250 mg t.i.w.–q.d. (Zithromax)</td>
<td>Tretinoin 0.025%/clindamycin phosphate 1.2% gel (Ziana)</td>
<td></td>
<td></td>
<td>Melaleuca alternifolia (tea tree oil) (topical)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clarithromycin 250 mg, 333 mg, 500 mg b.i.d.–q.d. (Biaxin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erythromycin 250–500 mg b.i.d.–q.i.d.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

q.d. = once daily; b.i.d. = twice a day; t.i.d = three times a day; t.i.w. = three times a week; q.i.d. = four times a day; mg = milligram; pad = pledget; sol = solution.

**Treatment**

Therapies for acne are varied and include proper cleaning regimens, topical agents, oral antibiotics, oral retinoids, and oral hormonal therapies. Available treatments are outlined in Table 2.

The skin of patients with acne can be easily irritated by topical agents that are used to treat the condition. The use of mild, non-drying cleaning products and non-comedogenic moisturizers may help reduce this irritation.

**Topical Therapies**

All topical medications dry the skin to some extent, and patients should be warned about this. They should be advised to use the medications as tolerated.

For example, the topical medication can be used for 15 minutes at a time and then washed off. The time can be increased as tolerated, or the agent can be used every other day or every third day, with the frequency to be increased as tolerated.
Antibiotics

The use of a topical agent is usually the best place to start treatment. The simplest and most cost-effective agent is benzoyl peroxide if it is tolerated. Bacterial resistance to benzoyl peroxide has not been noted. This agent can be used as a leave-on product or as a wash. It is available over the counter and by prescription in various topical forms, including pledgets, soaps, washes, lotions, creams, and gels. It is also available as part of combination products that also contain clindamycin (e.g., Benzaclin) or erythromycin (e.g., Benzamycin). It ranges in strength from 2.5% to 10%. However, more so than other topical acne treatments, benzoyl peroxide can induce allergic contact dermatitis.

Proactiv is an FDA-approved, OTC brand of benzoyl peroxide that has achieved prominence because of aggressive direct-to-consumer marketing. This benzoyl peroxide/sulfur combination can be more soothing for patients than traditional benzoyl peroxide products. It is available as a cleanser, toner, and repairing solution. The possibility of increased tolerability, its advertising campaign, and the basic effectiveness of benzoyl peroxide against acne have made Proactiv one of the most successful acne treatments ever, in terms of dollar volume.

Other acne medications include topical antibiotics whose active agent is erythromycin or clindamycin. Topical metronidazole, which is commonly used to treat rosacea, is not indicated for treating acne. These agents, like their oral counterparts, are particularly effective against inflammatory acne and acne related to P. acnes responds to topical or oral antibiotics. The FDA has approved dapsonate 5% gel (Aczone, QLT USA) to treat acne after glucose-6-phosphate dehydrogenase (G6PD) levels are assessed, as required in the product’s boxed warning. A phase 4 post-approval trial is currently ongoing with the goal of having the restriction removed. In a study of patients with G6PD deficiency, the gel was found to be safe and effective in substantially decreasing inflammatory acneiform lesions.

Antibiotics do not abate comedones, and bacterial resistance to antibiotics may develop. The development of resistance is reduced if topical antibiotics are used in combination with benzoyl peroxide.

Topical Retinoids

For mild acne, it is best to start with topical medications, which should be given for six to eight weeks. A first-line treatment for comedonal, non-inflammatory acne involves the use of topical retinoids (e.g., Retin-A), such as tretinoin, adapalene (Differin, Galderma), and tazarotene (e.g., Allergan’s Tazorac and Avage). Topical retinoids have comedolytic and anti-inflammatory properties. They increase epidermal differentiation and help normalize and abate follicular hyperproliferation and hyperkeratinization. Topical retinoids are the only medications that abate open and closed comedones; they decrease the quantity of micro-comedones, comedones, and inflammatory papules and pustules.

Retinoids are effective as monotherapy, or they can be combined with topical regimens that include antibiotics and benzoyl peroxide. Topical retinoids can also be used in conjunction with oral antibiotics.

Topical retinoids should be applied to clean, dry skin once daily. If they cause irritation, they can be applied every other day or every third day if irritation occurs with daily use. Some physicians have advocated the use of short-contact regimens with tazarotene, which is applied to the face for 5 to 20 minutes and is then removed by washing. Skin irritation, skin flaking and peeling, and redness of the skin can be linked to the use of topical retinoids.

Mild, non-drying skin cleaners and non-comedogenic moisturizers may help reduce this irritation. Alternate-day dosing may be used if irritation persists. Topical retinoids thin the stratum corneum, and they can be associated with sun sensitivity.

New developments in retinoids include a combination product of tretinoin 0.025% and clindamycin phosphate 1.2% in a gel (Ziana, Medicis). Ziana is indicated for the topical treatment of acne in patients 12 years of age and older.

According to trials, adapalene 0.3% gel (Differin) might be superior to its 0.1% gel predecessor.

A product combining tretinoin 0.025% and clindamycin phosphate 1% in a hydrogel base (Velac, Connetics) has not yet come to market.

Additional Topical Agents

Other topical agents include azelaic acid, either as a cream (Azelex, Allergan) or a gel (Finacea, Intendis), used once a day. Products that contain sulfur in different forms are soothing and somewhat effective for treating acne, rosacea, and seborrheic dermatitis.

Oral Therapies

Antibiotics

Oral antibiotics are effective in the treatment of acne, particularly when acne is related to inflammation or P. acnes infection. As previously stated, the antibiotics are useful for moderate and severe grades of inflammatory acne because of their anti-inflammatory properties.

Tetracyclines. Tetracyclines are commonly used to treat acne. Some authors think that more lipophilic antibiotics and antibiotics with less P. acnes resistance, such as minocycline (Minocin), are more effective than tetracycline. Others claim that there is no clear proof that minocycline is superior to tetracycline. Because tetracyclines stain the teeth, they should not be used in children.

Doxycycline. A new development in the role of oral antibiotics for acne treatment is the use of submicrobial doses of doxycycline (Vibramycin). These doses have only anti-inflammatory rather than antibiotic activity, and they have been shown to be equivalent to higher antimicrobial doses.

Erythromycin. Oral erythromycin has been a mainstay of anti-acne treatment. P. acnes resistance to erythromycin has greatly reduced its utility in acne therapy.

Azithromycin. Azithromycin (Zithromax) has been suggested as an effective acne treatment, and it might be more useful than erythromycin because of its longer half-life, greater anti-inflammatory activity, wider coverage of gram-negative organisms, and fewer gastrointestinal adverse effects. Irreversible deafness has been reported after the use of low-dose azithromycin in healthy patients, but the handful of cases suggests that this side effect is rare.
Sulfa agents. Trimethoprim/sulfamethoxazole (Bactrim), given as a double-strength tablet twice a day, can be effective; it often works when other antibiotics fail. It is useful in treating gram-negative folliculitis, a mimic of acne that does not respond to tetracycline or macrolides but does respond to isotretinoin and trimethoprim/sulfamethoxazole.

The most common adverse side effect is a maculopapular eruption; rare side effects include Stevens-Johnson syndrome, hepatitis, and toxic epidermal necrolysis.

The combination of methotrexate plus trimethoprim/sulfamethoxazole can be fatal. If patients are taking methotrexate for psoriasis or rheumatoid arthritis or if they intend to use methotrexate as an abortifacient and they seek treatment of acne, these drugs should not be prescribed together. For many dermatologists, these possible adverse effects make trimethoprim/sulfamethoxazole a third-line therapy for acne.

Oral Contraceptives

Oral contraceptives are effective in women for acne that is related to androgen excess or that waxes and wanes with their menstrual periods. These agents increase sex hormone–binding globulin; this decreases circulating free testosterone, thereby abating acne in some cases. Combination birth control tablets have shown efficacy in the treatment of acne vulgaris. Spironolactone (Aldactone), which may also be used in the treatment of acne vulgaris, binds the androgen receptor and reduces androgen production.

Oral Retinoids (Isotretinoin)

Isotretinoin (Accutane), a systemic retinoid, is the single most effective agent for the treatment of acne of all types. It normalizes epidermal differentiation and inhibits sebum excretion permanently by 70%. Isotretinoin also works as an anti-inflammatory agent. However, it is not a panacea; one study found that 7.2% of patients with acne did not respond to isotretinoin therapy.

Some dermatologists find that dispensing enough isotretinoin to achieve a cumulative dose of 120 to 150 mg/kg is the optimal way to use this agent for acne; they prefer that isotretinoin 1 mg/kg be given in a divided dose twice a day for five months or that therapy be initiated at a dose of 0.5 mg/kg per day for four weeks and increased as tolerated until a dose of 1 mg/kg daily is achieved. Other experts advocate the low-dose regimens of isotretinoin involving six months of treatment with 20 mg/day, noting that such dosing has a low incidence of severe side effects and is less expensive than higher-dose regimens.

As a rule, a single course of isotretinoin at a cumulative dose of 120 to 150 mg/kg should cure acne in two-thirds of patients. A side effect from the continued use of isotretinoin, however, is a condition known as diffuse idiopathic skeletal hyperostosis (DISH). For this reason, some physicians order a radiographical skeletal baseline examination if repeated courses of isotretinoin are considered. Patients should be warned of the rare possibility of the occurrence of DISH before therapy is begun.

Isotretinoin is a teratogen, and fertile women must be informed of this fact. In the U.S., isotretinoin may be distributed only if patients, physicians, and pharmacists participate in the iPledge program. Before pharmacists may distribute the product, patients must enroll in this program and a negative pregnancy test in fertile women must be confirmed.

Isotretinoin does not seem to have a negative effect on mood. Some reports suggest that it increases the incidence of depression, but larger studies have not borne this out. Children exposed to high doses of isotretinoin are at risk for premature epiphyseal closure, whereas adults maintaining long-term therapy have an increased tendency to develop hyperostosis and other changes in bones. In any case, physicians must counsel women regarding contraception, and two negative pregnancy test results are required before therapy can be initiated. These test results must be confirmed monthly.

For all patients, a baseline laboratory examination should also include assessments of cholesterol, triglyceride, and hepatic transaminase levels as well as a complete blood count. Although an increase of isotretinoin has been shown to raise triglyceride levels in well-documented cases, its adverse effects on the liver are less well defined and certainly less common.

In cases of acne fulminans, isotretinoin can worsen acne initially. Coadministration with corticosteroids at the beginning of therapy can be useful in severe cases to prevent the initial flaring of acne.

Nutritional Supplements

Vitamins and minerals have been used to treat acne. Pharmacological doses of nicotinamide tablets (e.g., Nicomide, DUSA/Sirus), 1.5 g/day, given in divided doses two or three times a day, have been used often in combination with zinc, copper, and folic acid. Oral and topical zinc have also been advocated, but strong evidence of its effect needs to be established.

Other Treatments

For variations of acne, other therapies can be attempted. Triamcinolone. Cysts of acne respond within a day after injections with triamcinolone acetonide (Kenalog, Apothecon) at a concentration of 2 to 3 mg/mL, although atrophy can result temporarily. Recently, lasers and light sources have been advocated, but controlled studies are lacking and such treatments are expensive.

Psychotropic medications. Acne excoriée is characterized by excessive scratching or picking of normal skin or skin with minor surface irregularities. It is most common in young women who pick at scattered acne papules, which are turned into scars. The compulsion is best treated with antidepressants or antipsychotic medications combined with isotretinoin. Medications that can be used include the selective serotonin reuptake inhibitors (SSRIs) as first-line psychiatric agents (e.g., Zoloft, Paxil, or Prozac). If the obsessive–compulsive ability is severe, low-dose risperidone (Risperdal, Janssen) 2 mg or olanzapine (Zyprexa, Eli Lilly) 2.5 mg can be helpful. It may be advisable for patients to seek out psychological assistance or counseling in these cases.

Surgery. Acne surgery involves the extraction of comedones. Open comedones are pores that contain keratin plugs with black tops (blackheads). Closed comedones are pores containing keratin plugs with white tops that may be more firmly embedded than open comedones (whiteheads). Comedones are not usually inflamed, but they can be.
How Long Should Therapy Continue?

Acne naturally waxes and wanes, and the use of therapy can be instituted and discontinued as needed. After the inflammation is controlled with oral antibiotics, acne can often be controlled with topical retinoids and benzoyl peroxide for long periods. Long-term therapy with minocycline beyond six months carries an increased risk of pigmentary deposition. Many acne patients continue with an antibiotic for more than a year without adverse effects. Isotretinoin can “cure” acne in many cases, although up to 20% to 25% of patients need to be re-treated for optimal results. Topical retinoids have anti-aging effects on the skin; thus, long-term therapy, if tolerated, can be seen as desirable.

Role of the Pharmacist

Pharmacists play an important role in acne treatment. They must be aware of the side effects of acne medications and the potential interactions of acne medications with other agents, in particular methotrexate and sulfamethoxazole/trimethoprim. Pharmacists are active participants in the pI pledge program and must use an online database to disburse isotretinoin.

Many patients with acne never see a physician, and they often seek advice from a pharmacist about therapy. In an Australian study by Yeatman et al., 70% of the 315 consumers interviewed were purchasing OTC products, and 50% purchased prescription items. Of the OTC products, 42% were originally recommended by the pharmacy staff members and 18% were recommended by doctors. More than one-third of consumers buying OTC products described symptoms to the pharmacy staff, and in about 50% of cases, they spoke to the pharmacy assistant. Pharmacists must be aware of different OTC preparations, including benzoyl peroxide, salicylic acid, sulfur, and sodium sulfacetamide, all of which are available in concentrations of 2% or more.

Conclusion

Acne continues to be one of the most common diseases in the U.S. Treatments have greatly improved the quality of life for patients. In particular, isotretinoin has been useful in severe cases. However, the new pI pledge program has limited the use of prescribing medications. Submicrobial doses of doxycycline, topical dapsona, and adapalene 0.3% cream are promising new modalities.

Acne is a disease with substantial morbidity that can be ameliorated with treatment and that requires the partnership of the patient, physician, and pharmacist to achieve its greatest effectiveness.

References


Continuing Education Questions for Physicians and Pharmacists

*P&T*® 2007;32(6):340–347

**ACPE Program # 079-999-07-018-H04**

**Expiration Date: June 30, 2008**

**TOPIC: Acne: A Review of Diagnosis and Treatment**

---

**CME Accreditation**

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Jefferson Medical College and MediMedia USA, Inc.

Jefferson Medical College of Thomas Jefferson University, as a member of the Consortium for Academic Continuing Medical Education, is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. All faculty/authors participating in continuing medical education activities sponsored by Jefferson Medical College are expected to disclose to the activity audience any real or apparent conflict(s) of interest related to the content of their article(s). Full disclosure of these relationships appears on the last page of the article.

---

**Continuing Medical Education Credit**

This CME activity is designed to assist physicians and other health care professionals who are P&T committee members in making formulary decisions. Its goal is to increase participants’ ability to recognize and treat important medical problems.

Jefferson Medical College designates this continuing medical education activity for a maximum of one Category 1 credit toward the Physician’s Recognition Award (PRA) of the American Medical Association. Each physician should claim only those credits that he/she actually spent in the educational activity.

This credit is available for the period of one year from the date of publication.

Although forms will be processed when received, certificates for CME credits will be issued every six months, in February and August. Interim requests for certificates can be made by contacting the Jefferson Office of Continuing Medical Education at (215) 955-6992 or by going online to [http://jeffline.tju.edu/jeffcme/](http://jeffline.tju.edu/jeffcme/).

---

**Continuing Pharmacy Education Credit**

The Department of Health Policy, Thomas Jefferson University Hospital, is approved by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education and complies with the Criteria for Quality for continuing pharmacy education programming. This program (079-999-07-018-H04) is acceptable for 1.0 hour of continuing education credit (0.1 CEUs) in states that recognize ACPE-approved providers. Statements of Credit indicating hours/CEUs will be mailed within six to eight weeks to participants who completed this activity and submitted a completed evaluation with payment.

---

**How to Apply for CE Credit**

1. Each CE article is prefaced by learning objectives for participants to use to determine whether the article relates to their individual learning needs.
2. Read the article carefully, paying particular attention to the tables and other illustrative materials.
3. Complete the questions and fill in the answers on the evaluation form on the next page.
4. Complete the CE Registration and Evaluation Form. Type or print your full name and address in the space provided, and evaluate the activity as requested. In order for the form to be processed, all information must be complete and legible.
5. Payment of $10 per exam is required for processing and maintenance of records. Make checks payable to *P&T*®. This processing fee is non-refundable.
6. Send the completed form, answer sheet, and $10 payment to:
   - Department of Health Policy
   - Thomas Jefferson University
   - Attn: Continuing Education Credit
   - 1015 Walnut Street, Suite 115
   - Philadelphia, PA 19107
7. Be sure to mail the Registration, Evaluation Form, and $10 payment within one year of the date of publication. After that date, this article will no longer be designated for credit and forms cannot be processed.
Continuing Education Questions for Physicians and Pharmacists

**TOPIC: Acne: A Review of Diagnosis and Treatment**

APCE Program # 079-999-07-018-H04

**Multiple Choice**

Select the one correct answer.

1. Which of the following is correct regarding the epidemiology of acne?
   a. Acne occurs primarily in men in their later years.
   b. Acne occurs most commonly in women in the postmenopausal phase.
   c. Acne is the least common dermatological condition in the U.S.
   d. Acne affects almost all humans at some point in their lives, and approximately seven million new cases are diagnosed each year in the U.S.

2. Pharmacists are often on the front lines of care for acne patients seeking relief.
   a. True
   b. False

3. Which of the following is correct in regard to the clinical presentation of acne?
   a. comedones on the face
   b. papules and pustules of the face, chest, and back
   c. pain, tenderness, and erythema around cysts
   d. all of the above

4. Which of the following is/are associated with an increased risk of developing (worsening) acne?
   a. menstrual period and hormonal imbalances
   b. fatty foods
   c. oral medications (i.e., trazodone, haloperidol, estrogen, phenytoin)
   d. all of the above

5. The nonpharmacological management of acne may include which of the following?
   a. isotretinoin
   b. tetracycline
   c. doxycycline
   d. benzoyl peroxide

6. Which of the following is true regarding the role of over-the-counter medications in the management of acne?
   a. Doxycycline is the most cost-effective treatment.
   b. Oral OTC medications are the most common and effective treatment.
   c. Patients should not combine OTC medications and prescription medication for acne.
   d. Benzoyl peroxide is the simplest and most cost-effective treatment if tolerated.

7. Which of the following patients are poor candidates for OTC medications for acne?
   a. patients with only comedones on the face
   b. patients with papules, pustules, and comedones on the face
   c. patients with papules and pustules on the face
   d. patients with papules, pustules, and cysts on the face, chest, neck, and back

8. When counseling acne patients who have chosen to use isotretinoin for acne management, which of the following statement(s) is/are correct?
   a. Patients should be warned of the rare possibility of the occurrence of diffuse idiopathic skeletal hyperostosis (DISH).
   b. Patients are required to confirm a negative pregnancy test before pharmacists may distribute isotretinoin.
   c. A cumulative dose of 120 to 150 mg/kg is the optimal way to use isotretinoin for acne.
   d. all of the above

9. Oral contraceptives are effective in both women and men for acne that waxes and wanes periodically.
   a. True
   b. False

10. Which of the following is the rare side effect of trimethoprim/sulfamethaxazole?
    a. red man syndrome
    b. Stevens–Johnson syndrome
    c. Franson syndrome
    d. Raynaud syndrome
CE Registration and Evaluation Form

Date of publication: June 2007
Title: Acne: A Review of Diagnosis and Treatment
Authors: Noah S. Scheinfeld, JD, MD
Submission deadline: June 30, 2008
ACPE Program # 079-999-07-018-H04

Registration

Name: ____________________________________________________________ Degree: ____________________________________
Street address: ______________________________________________  Last 4 Digits of Social Security No. (Web ID): __________
City: ___________________________________  State: _________  Zip:__________  Telephone: _____________________________
E-mail Address: _______________________________________   Check one:

II  Physician
II  Pharmacist
II  Other

Time needed to complete this CE activity in hours: □ 0.5 hr  □ 1 hr  □ 1.5 hr  □ 2 hr  □ Other _________________________

Certification: I attest to having completed this CE activity. ___________________________________________________________
Signature (required) Date _______________

Answer Sheet

Please fill in the box next to the letter corresponding to the correct answer

1. a □ b □ c □ d □  6. a □ b □ c □ d □
2. a □ b □ c □ d □  7. a □ b □ c □ d □
3. a □ b □ c □ d □  8. a □ b □ c □ d □
4. a □ b □ c □ d □  9. a □ b □ c □ d □
5. a □ b □ c □ d □ 10. a □ b □ c □ d □

Evaluation

Rate the extent to which:

<table>
<thead>
<tr>
<th>Very High</th>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
<th>Very Low</th>
</tr>
</thead>
</table>
1. Objectives of this activity were met | ❑ | ❑ | ❑ | ❑ | ❑ |
2. You were satisfied with the overall quality of this activity | ❑ | ❑ | ❑ | ❑ | ❑ |
3. Content was relevant to your practice needs | ❑ | ❑ | ❑ | ❑ | ❑ |
4. Participation in this activity changed your knowledge/attitudes | ❑ | ❑ | ❑ | ❑ | ❑ |
5. You will make a change in your practice as a result of participation in this activity | ❑ | ❑ | ❑ | ❑ | ❑ |
6. This activity presented scientifically rigorous, unbiased, and balanced information | ❑ | ❑ | ❑ | ❑ | ❑ |
7. Individual presentations were free of commercial bias | ❑ | ❑ | ❑ | ❑ | ❑ |
8. Adequate time was available for Q&A | ❑ | ❑ | ❑ | ❑ | ❑ |
9. Which ONE of the following best describes the impact of this activity on your performance:
   □ This program will not change my behavior because my current practice is consistent with what was taught.
   □ This activity will not change my behavior because I do not agree with the information presented.
   □ I need more information before I can change my practice behavior.
   □ I will immediately implement the information into my practice.

10. Will you take any of the following actions as a result of participating in this educational activity (check all that apply)
   □ Discuss new information with other professionals
   □ Consult the literature
   □ Discuss with industry representative(s)
   □ Participate in another educational activity
   □ Other _________________________  □ None

Send the completed form and $10 payment (make checks payable to P&T) to: Department of Health Policy, Thomas Jefferson University, Attn: Continuing Education Credit, 1015 Walnut Street, Suite 115, Philadelphia, PA 19107.

Send the completed form and $10 payment (make checks payable to P&T) to: Department of Health Policy, Thomas Jefferson University, Attn: Continuing Education Credit, 1015 Walnut Street, Suite 115, Philadelphia, PA 19107.