



A SUPPLEMENT TO

Skin & Allergy News®



SKIN DISEASE
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Maximizing Results in the Treatment of Acne and Improving Facial Appearance

**Evidence-Based Results With
Topical Retinoids for Acne**

**The Use of Topical Retinoids With Combination
Therapies in the Management of Acne Vulgaris**

**How to Optimize Topical Retinoid/Oral
Antibiotic Therapy in Acne**

**State-of-the-Art Therapies for
Aging and Photoaging of the Skin**



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Annual Hawaii Dermatology Seminar*

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CME RECOGNITION

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TARGET AUDIENCE

This activity has been developed for dermatologists and other healthcare professionals involved in the treatment of facial acne vulgaris or in facial aesthetics.

EDUCATIONAL NEEDS

Maximizing Results in the Treatment of Acne and Improving Facial Appearance is a continuing medical education activity for dermatologists. The goals of this supplement are twofold. One goal is to update dermatologists on the use of topical retinoids, both as monotherapy and in combination therapy, in the treatment of facial acne vulgaris. The other goal is to discuss the beneficial effects of antioxidant and topical retinoid therapy in reducing the effects of skin aging.

LEARNING OBJECTIVES

After reading this supplement, participants should be able to:

- Compare and contrast the efficacy and tolerability of different topical retinoids used in the treatment of acne vulgaris.
- Evaluate the benefits of using an antibiotic and/or benzoyl peroxide adjunctively with a topical retinoid in the treatment of acne vulgaris.
- Describe how to optimize the use of topical retinoid and oral antibiotic therapy in acne vulgaris.
- Discuss how the effects of skin aging can be reduced using state-of-the-art antioxidant and topical retinoid products.

FACULTY AND UNAPPROVED USE DISCLOSURES

Faculty/authors must disclose any significant financial interest or relationship with proprietary entities that may have a direct relationship to the subject matter. They must also disclose any discussion of investigational or unlabeled uses of products.

Dr Downie is a consultant to and owns stock in Allergan, Inc. She discusses the unlabeled use of Retin A for photodamage. **Dr Green** is a consultant to Allergan. **Dr Tanghetti** has received funding for clinical grants and is a consultant to Allergan and Stiefel Laboratories, Inc. **Dr Thiboutot** has served as an investigator in clinical trials sponsored by and is on the Advisory Board at Allergan, Galderma S.A., and OrthoNeutrogena.

Evidence-Based Results With Topical Retinoids for Acne

Lawrence J. Green, MD

The Evolution of Topical Retinoid Therapy

The potential usefulness of retinoids for treating acne was recognized more than 50 years ago.¹ As early as the 1940s, oral vitamin A was reported to improve acne,¹ and, in the 1960s, Kligman et al reported the results of a clinical trial showing that topical vitamin A acid (tretinoin) was effective in reducing the overall lesion count and comedones in particular.² This landmark study heralded the beginning of an era where topical retinoids came to be known as “comedone busters.” Kligman’s study compared tretinoin (0.1% in an alcohol-based formulation) with other treatment options available at the time in patients whose acne consisted predominantly of comedonal lesions. The results of the study demonstrated that this tretinoin formulation achieved a greater reduction in overall lesion count than either 5% benzoyl peroxide or 5% sulphur/3% resorcinol lotion (two topical treatments often

“Tazarotene cream is better tolerated than is tazarotene gel, adapalene gel is better tolerated than is adapalene cream, and tretinoin microsp sponge is better tolerated than is tretinoin cream.”

used at that time). Thus, this formulation of tretinoin was shown not only to be efficacious but also to offer superior efficacy against other treatment options.

In the 1970s, tretinoin (once-daily 0.05% cream) was shown to be efficacious against inflammatory lesions as well as comedones, and it became apparent that the clinical utility of tretinoin was not limited to the treatment of comedonal acne.³ More than 15 years later, in the late 1990s, two novel topical retinoids—tazarotene and adapalene—were

approved by the US Food and Drug Administration for the treatment of acne. The receptor selectivity of these retinoids was hypothesized to help enhance tolerability relative to tretinoin (which is not as receptor selective). A new microsp sponge formulation of tretinoin was also introduced in an attempt to minimize tolerability issues with tretinoin. The introduction of two new retinoids and several new formulations widened the treatment options available and necessitated comparative evaluations of efficacy and tolerability.

Efficacy comparisons

The results from a series of 12-week multicenter, double-blind, randomized, parallel-group trials involving more than 600 patients in total have shown that tazarotene offers superior efficacy to that of other retinoids regardless of which formulation is used. Thus, tazarotene 0.1% gel has been shown to offer superior efficacy to that of adapa-

Figure 1. Reduction in comedone count after 12 weeks of topical retinoid therapy (all data from multicenter, double-blind, randomized, parallel-group trials).⁴⁻⁷

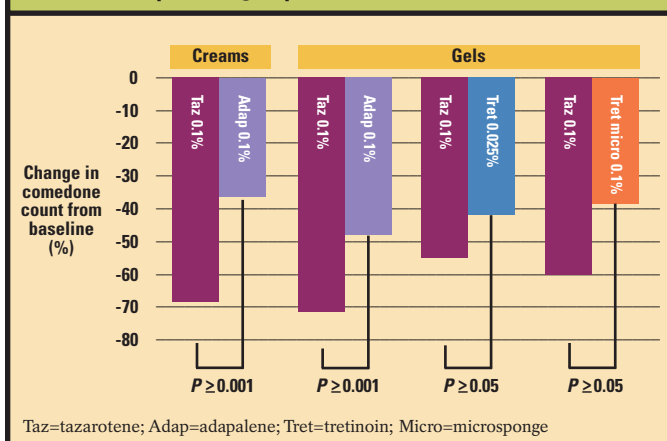
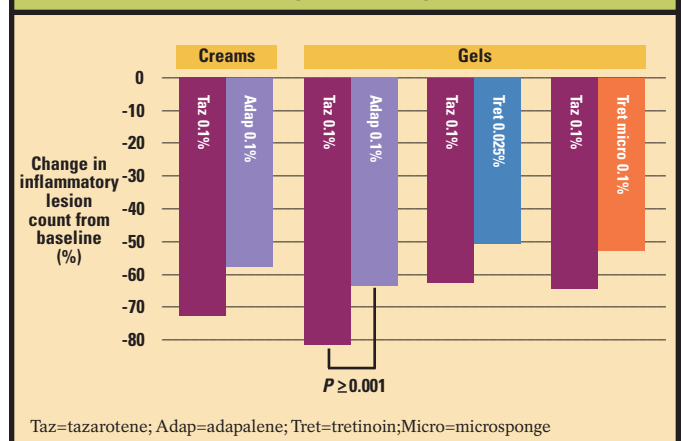


Figure 2. Reduction in inflammatory lesion count after 12 weeks of topical retinoid therapy (all data from multicenter, double-blind, randomized, parallel-group trials).⁴⁻⁷



lene 0.1% gel, tretinoin 0.025% gel, and tretinoin 0.1% microsphere gel (Figures 1 and 2).⁴⁻⁶ Similarly, tazarotene 0.1% cream has been shown to offer superior efficacy to adapalene 0.1% cream (Figure 1).⁷

Alternate-day applications of tazarotene 0.1% gel have also been shown to be as effective as once-daily applications of adapalene 0.1% gel.⁸ Furthermore, both alternate-day and once-daily applications of tazarotene 0.1% gel have been

demonstrated to be more cost-effective treatment options than is once-daily adapalene 0.1% gel.^{4,9}

“Tazarotene offers superior efficacy to that of other retinoids.”

Tolerability Comparisons

The results of split-face studies have demonstrated that tolerability may be influenced by the concentration of the retinoid, the sensitivity of the patient’s skin, the vehicle used in the formulation, and the choice of retinoid.¹⁰ As might be expected, tolerability is optimal with lower- rather than higher-concentration formulations and in patients with normal skin rather than sensitive skin. The vehicle with the best tolerability depends on which retinoid is being evaluated—tazarotene cream is better tolerated than is tazarotene gel, adapalene gel is better tolerated than is adapalene cream, and tretinoin microsphere gel is better tolerated than is tretinoin cream.

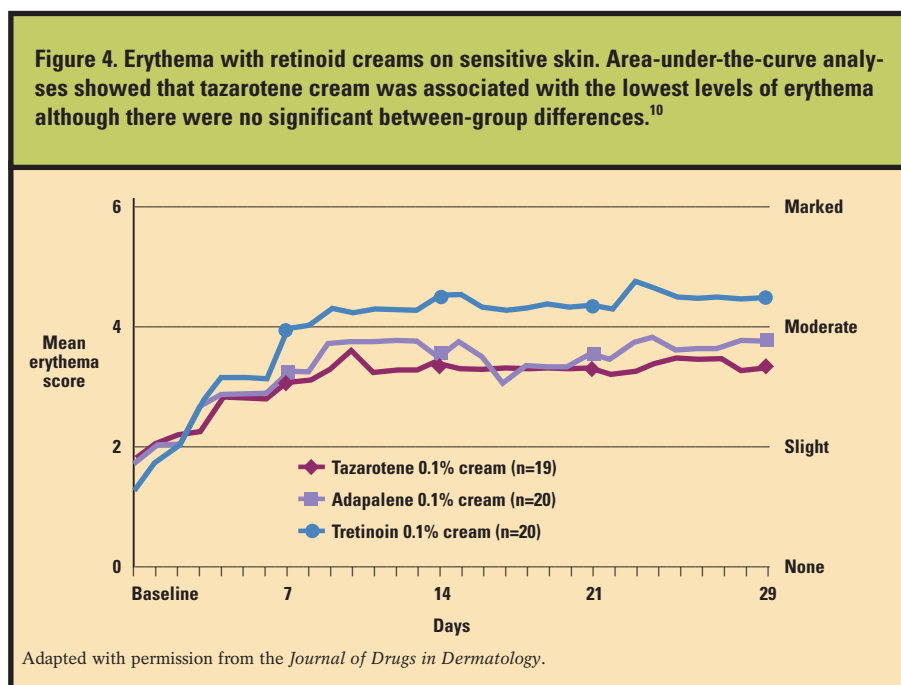
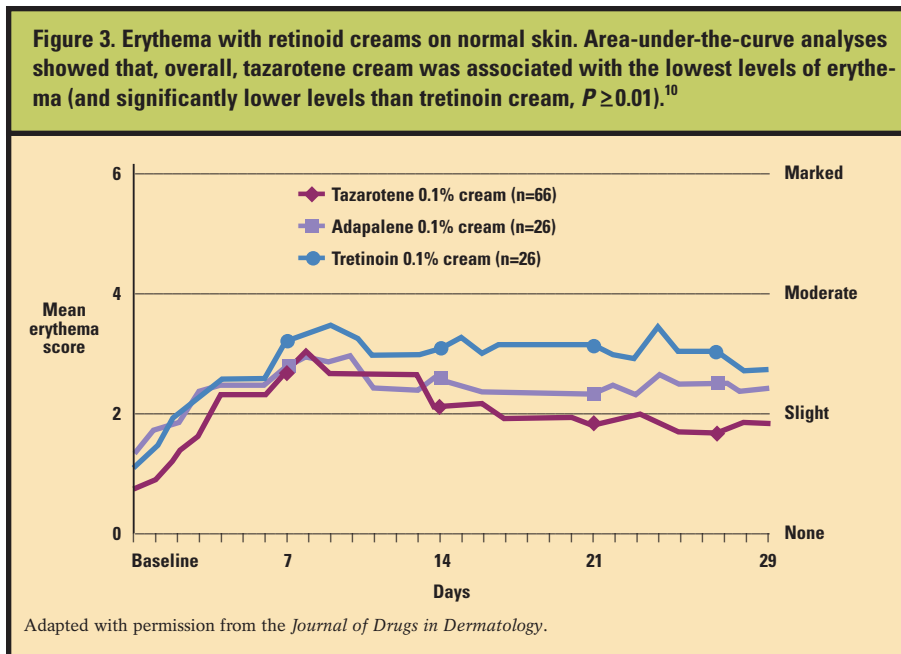
When retinoid creams were compared, the overall levels of erythema and dryness were lower with tazarotene 0.1% cream than with adapalene 0.1% cream or tretinoin 0.1% cream both on normal and on sensitive skin (Figures 3 and 4).¹⁰ These differences reached statistical significance versus tretinoin 0.1% cream for both erythema (Figure 3) and dryness on normal skin and for dryness (but not erythema) on sensitive skin.

When retinoid gels were compared, the overall levels of erythema and dryness were lower with adapalene 0.1% gel than with tazarotene 0.1% gel or tretinoin 0.1% microsphere gel on both normal and sensitive skin. These differences reached statistical significance versus tazarotene 0.1% gel for erythema and dryness only on normal skin.

Future Trends in Topical Retinoid Therapy

Although the efficacy of topical retinoid therapy in both inflammatory and comedonal acne was evident in the early years, initially it was used primarily for comedonal acne and was often overlooked for inflammatory acne. Today, it is

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The Use of Topical Retinoids With Combination Therapies in the Management of Acne Vulgaris

Emil A. Tanghetti, MD

Topical retinoids are highly effective against both comedonal and inflammatory acne. They help resolve comedonal acne by promoting normalization of follicular epithelial desquamation, which encourages comedonal drainage and helps prevent the development of new comedones. The efficacy of topical retinoids against inflammatory acne may be partly a consequence of this comedonal drainage (which helps create a less favorable follicular microenvironment for *Propionibacterium acnes*) and partly a consequence of inhibiting the expression of toll-like receptors on monocytes and macrophages (which results in reduced expression of proinflammatory cytokines).¹

Enhancing the Efficacy of Topical Retinoids

Although topical retinoids are highly effective, it is conceivable that their efficacy could be enhanced still further through the adjunctive use of other antiacne agents with complementary mechanisms of action (eg, antibiotics and benzoyl peroxide, which also reduce the proliferation of *P. acnes*). Although the primary mechanism of action of antibiotic/benzoyl peroxide products is antibacterial, this antibacterial action also reduces the release of comedogenic and inflammatory products from *P. acnes*—which, in turn, lowers the potential for the development of comedones and inflammatory lesions. Benzoyl peroxide, in particular, has been reported to have comedolytic activity,^{2,4} and clindamycin/benzoyl peroxide has been shown to result in signifi-

“Adjunctive use of clindamycin/benzoyl peroxide can significantly increase the reduction in both inflammatory lesions and comedones achievable with tazarotene.”

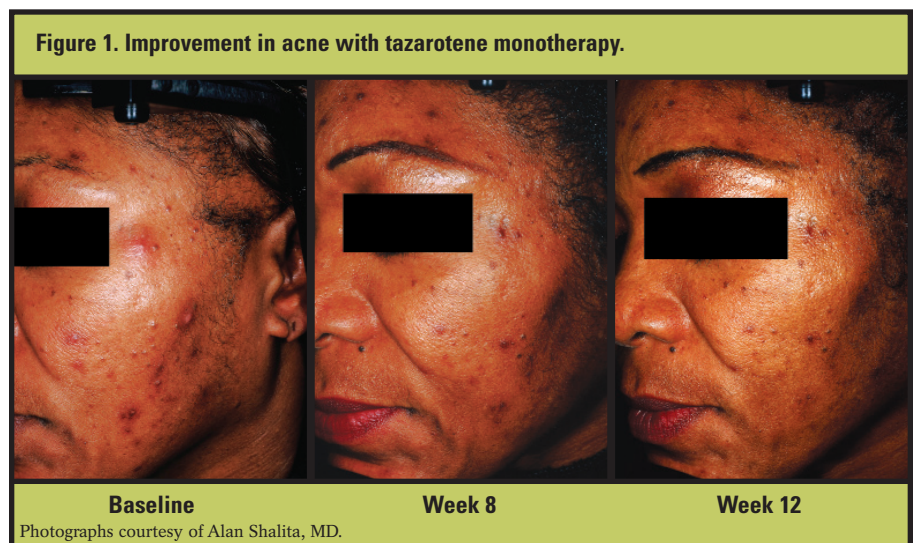
cantly greater reductions in comedonal lesions (as well as inflammatory lesions) than has clindamycin alone.⁵

Adjunctive Use of an Antibiotic/Benzoyl Peroxide Product With a Topical Retinoid

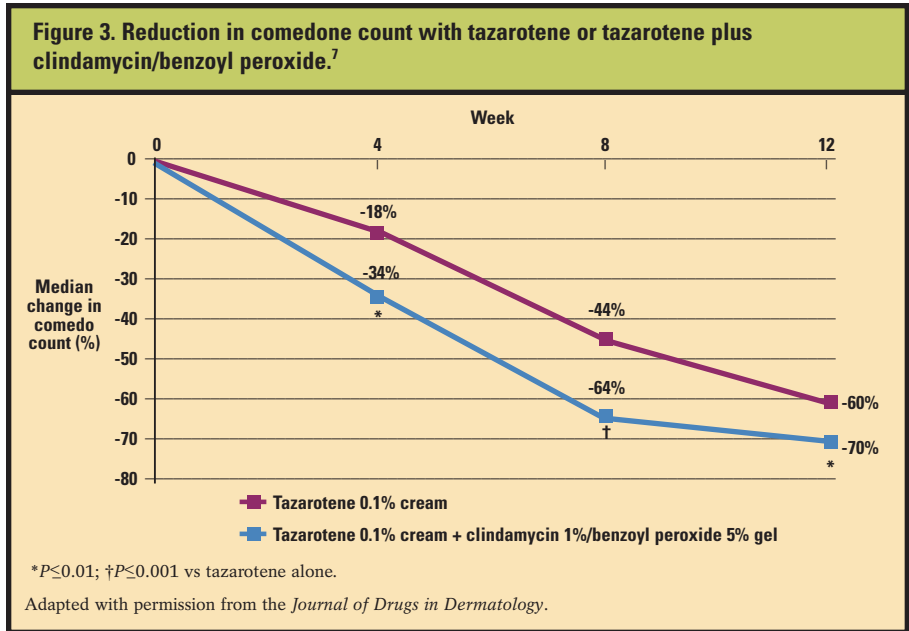
There are few studies in the literature describing combination therapy with a retinoid and an antibiotic/benzoyl peroxide. One community-based study involving 440 patients with mild to moderate acne vulgaris reported that the adjunctive use of erythromycin/benzoyl peroxide sig-

nificantly increased the reduction in inflammatory lesion count achievable with tazarotene 0.1% gel but did not increase the reduction in comedone count.⁶ The adjunctive use of benzoyl peroxide alone or clindamycin alone did not enhance the efficacy of tazarotene against either type of acne. Although the data on inflammatory lesions from this trial should be reliable, it is possible that the accuracy of the comedone counts could have been compromised by the community setting of this trial—comedones are harder to count accurately than are inflammatory lesions, and many of the more than 40 investigators involved were not routinely involved in assessing comedone counts in a research setting.

Recently, the results of another trial have demonstrated that the adjunctive use of clindamycin 1%/benzoyl peroxide 5% gel (a ready-to-dispense formulation containing two emollients) can significantly ($P \leq 0.01$) increase the reduc-



tion in both inflammatory lesions and comedones achievable with tazarotene 0.1% cream (Figures 1 and 2).⁷ In this trial of 121 patients with moderate to severe facial acne, once-daily applications of tazarotene (in the evening) plus clindamycin/benzoyl peroxide (in the morning) resulted in significantly greater anticomedonal efficacy—as well as faster efficacy—than did tazarotene alone. The reduction in comedones was significantly greater with tazarotene plus clindamycin/benzoyl peroxide than with tazarotene alone as early as week 4, and the significant between-group difference continued through the end of the study. At week 12, the reduction in comedones was a mean of 60% with tazarotene alone and 70% with tazarotene plus clindamycin/benzoyl peroxide (Figure 3, $P \leq 0.01$).⁷ Furthermore, tolerability was at least as good with the combination therapy as with tazarotene alone (the incidences of peeling and dryness were both lower with combination therapy than with monotherapy, although statistical significance was not achieved). This possible improvement in tolerability may be due to the clindamycin/benzoyl peroxide specifically, or it may be related to the emollient vehicle in which the product used in the study was formulated. (The formulation



used contains the emollients glycerin and dimethicone.)

Although perhaps unexpected, possible improvements in tolerability have been reported previously when topical retinoids are used in combination therapy rather than as monotherapy. In the study with erythromycin/benzoyl peroxide mentioned above, the incidences of peeling and dryness were not specifically reported, but the incidence of discontinuations due to adverse events was lower with tazarotene plus erythromycin/benzoyl peroxide than with tazarotene alone (6% vs 11%, respectively).⁶ The incidence of discontinuations due to adverse events

was also lower with other combinations (tazarotene plus clindamycin [5%] or tazarotene plus benzoyl peroxide [7%]) than with tazarotene alone. Less irritation has also been reported when tretinoin is used in conjunction with benzoyl peroxide than when used alone.⁸

“Tolerability may also be enhanced by combination therapy.”

Summary

A topical retinoid plus adjunctive use of an antibiotic/benzoyl peroxide product can be appropriate first-line therapy for both comedonal and inflammatory acne. Such therapy targets three of the four factors known to be involved in the pathogenesis of acne—abnormal desquamation of the follicular epithelium, inflammation, and proliferation of *P. acnes*—and therefore should offer excellent efficacy. Furthermore, perhaps a little unexpectedly, tolerability may also be enhanced by combination therapy. The results of the study with tazarotene and clindamycin/benzoyl peroxide provide further supportive evidence for the

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How to Optimize Topical Retinoid/Oral Antibiotic Therapy in Acne

Diane Thiboutot, MD

Topical retinoids are the mainstay of therapy for both inflammatory and noninflammatory acne as they help prevent the development of microcomedones—the precursors of all other acne lesions. Their ability to help normalize follicular desquamation promotes comedolytic activity and prevents follicular blockage. Recent research also suggests that topical retinoids have direct immunomodulatory effects that may contribute to their activity against inflammatory lesions—for example, stimulation of interleukin-5 release and inhibition of interferon- γ release by superantigen-stimulated human peripheral blood mononuclear cells¹ and inhibition of the expression of toll-like receptor 2.²

Primary Therapy

Recently published consensus recommendations on the management of acne advocate the use of topical retinoids as primary therapy in most forms of acne, with adjunctive antimicrobial therapy when inflammatory acne lesions are present (Table 1).³ As topical retinoids and antimicrobials have different mechanisms of action, this provides a greater range of pathophysiologic targets than would be feasible with either as monotherapy. It is known that topical retinoid plus oral antibiotic therapy results in greater, and more rapid, reductions in *Propionibacterium acnes* counts and free fatty acid levels than does either agent alone.⁴ As a result, such combination therapy is highly valuable in optimizing efficacy and the speed of clinical improvement. It may be that the retinoid indirectly augments

“Maintenance strategies for acne should aim to minimize the long-term use of antibiotics.”

the efficacy of the antibiotic as a result of increasing vascular permeability, resulting in enhanced delivery of the antibiotic to the interstitial fluid compartment of the dermis.⁴ The retinoid-induced increase in cell turnover of the follicular epithelium may also facilitate greater transport of the antibiotic into the follicular canal.

Maintenance Therapy

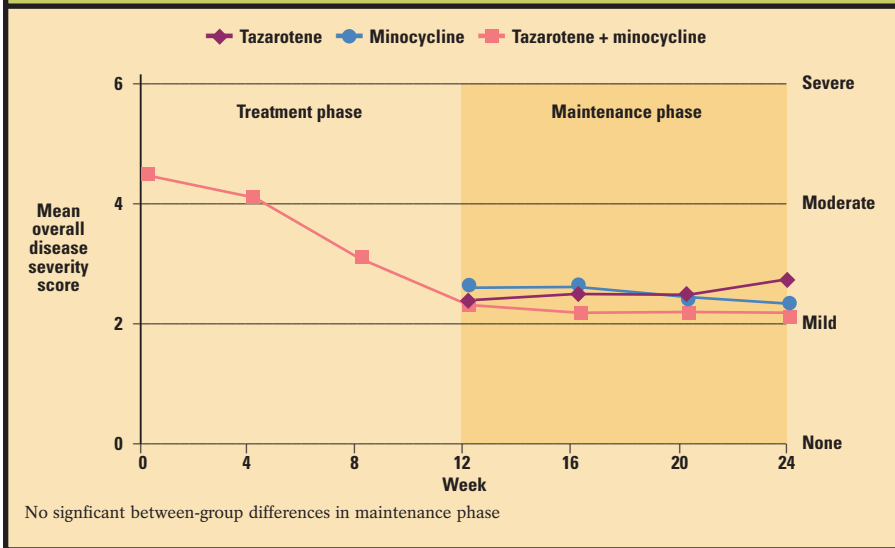
Although the advantages of using oral antibiotics in early treatment are evident, the prolonged use of oral antibiotics is undesirable for several reasons. First, many patients prefer to minimize their exposure to

oral medications in general and oral antibiotics in particular. Second, recent research raised concern when it was suggested that long-term exposure to antibiotics may be associated with an increased risk of breast cancer.⁵ Third, the resistance of *P. acnes* to antibiotics is a growing problem (the overall incidence of such resistance increased from 20% to 62% between 1978 and 1996),⁶ and the potential transfer of antibiotic resistance to other bacteria against which these drugs are used is a major concern. Resistant *P. acnes* are widely distributed not only on acne-prone skin but also in the nares.⁷ Because of this, it is likely that these bacteria (and particularly those in the nasal reservoir) are hard to eradicate with existing therapeutic regimens, and so our attention must be focused on prevention. To help minimize the development of *P. acnes* resistance, the consensus group of experts has recommended that maintenance strategies for acne

Table 1. Key consensus recommendations for the management of acne³

- > Topical retinoids should be the primary treatment for most forms of acne vulgaris
- > Use early (at the onset of therapy) for greatest and fastest results
- > Combine with antimicrobial therapy when inflammatory lesions are present
- > Clearing of both inflammatory lesions and comedones is faster and significantly greater with combination therapy than with antibiotic therapy alone
- > The antibiotic should be discontinued when inflammatory lesions resolve adequately
- > Topical retinoids are an essential part of maintenance therapy
- > Continue use of the topical retinoid to maintain remission when antibiotic therapy is discontinued

Figure 1. Mean overall disease severity score.⁹



“...an important option to consider in patients who might otherwise be prescribed oral isotretinoin.”

should aim to minimize the long-term use of antibiotics.³

Topical retinoids are the treatment of choice for maintenance therapy because of their ability to prevent the development of microcomedones,⁸ and it is possible that topical retinoid therapy alone may provide sufficient efficacy for maintenance therapy. To evaluate the clinical potential of such treatment, a study has been performed to compare the efficacy of three maintenance therapies (tazarotene alone, minocycline alone, and tazarotene plus minocycline) in sustaining the clinical improvement attained after initial tazarotene plus minocycline therapy. In this study of 189 patients with moderate to severe inflammatory acne, all patients were initially treated for 12 weeks with once-daily tazarotene 0.1% gel plus twice-daily minocycline 100-mg capsules.⁹ Patients who had achieved at least a 75% global improvement at week 12 were eligible to enter the double-blind, randomized, maintenance phase, in which they were assigned treatment with tazarotene alone, minocycline alone, or tazarotene plus minocycline for an additional 12 weeks. The results of the study show that all three regimens were highly effective maintenance therapies. There were no significant between-group differences in overall disease severity at any timepoint during the maintenance phase (Figure 1) and between 80% and 90% of patients in each group sustained at least 50% global improvement from baseline through the end of the 12-week maintenance phase.⁹ Figure 2 shows the excellent maintenance of clinical improvement that

Figure 2A. Improvement in acne with tazarotene plus minocycline therapy (from baseline to week 12) and sustained improvement with tazarotene monotherapy maintenance therapy (from week 12 to week 24).⁹



Figure 2B. Improvement in acne with tazarotene plus minocycline therapy (from baseline to week 12) and sustained improvement with tazarotene monotherapy maintenance therapy (from week 12 to week 24).



can be achieved with tazarotene monotherapy.⁹

The results of this study suggest that, after good clinical improvement in acne has been attained with initial tazarotene plus minocycline therapy, tazarotene alone offers sufficient efficacy for ongoing maintenance therapy. (In everyday clinical practice, a gradual tapering of the antibiotic would likely offer the smoothest transition between initial and maintenance treatments.) Clinically, the results have two important implications. First, by helping avoid long-term exposure to antibiotics, the use of tazarotene monotherapy as maintenance therapy should help minimize the development of antibiotic-resistant *P. acnes*. Second, the high degree of efficacy demonstrated against moderate to severe inflammatory acne in both the initial and the maintenance phases suggests that the approach described here is an important option to consider in patients who might otherwise be prescribed oral isotretinoin.

“Topical retinoids are the treatment of choice for maintenance therapy.”

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State-of-the-Art Therapies for Aging and Photoaging of the Skin

Jeanine B. Downie, MD, FAAD

Skin aging can occur as a result of both genetics and environmental factors. Free radicals are thought to play a role in the aging process, and their production in their body can be accelerated by many factors, including exposure to the sun, cigarette smoke, and stress. To minimize aging of the skin, it is important to protect it from these stressors. In terms of skin care regimens, this means that the use of sunscreens and topical antioxidants is essential. A range of effective sunscreens have been available for many years, but research in the field of antioxidants is still progressing rapidly.

The need for a standardized method to compare various effects of antioxidants

Although antioxidants have demonstrated antioxidative and photoprotective properties in various *in vitro* and *in vivo* studies, a standardized method to characterize and compare the complex properties and effects of different topical antioxidants has been lacking. The topical antioxidants that are currently most popular are very heterogeneous in structure and origin, and a standardized protocol to compare them therefore needs to consist of a variety of evaluations to gain the broadest possible perspective on their effects. A protocol has been developed whereby the results of five *in vitro* or *in vivo* evaluations are combined to give an overall score reflecting the capacity of an antioxidant to protect against oxidative stress.¹ The five evaluations assess the following: human sunburn cell count after ultraviolet (UV) radiation, free radical scavenging

activity, primary products of lipid oxidation, secondary products of lipid oxidation, and byproducts of UV radiation in nuclei of human keratinocytes. The overall score obtained from the results of these evaluations is termed the Environmental Protection Factor—in line with the terminology for Sun Protection Factor and Immune Protection Factor.²

“A standardized method to characterize and compare the complex properties and effects of different topical antioxidants has been lacking.”

Comparing Idebenone With Other Topical Antioxidants

Recent research indicates that idebenone is a particularly potent and effective antioxidant. It is a synthetic analog of naturally occurring coenzyme Q10 but has a considerably lower molecular weight (338 versus 863), which may help enhance its penetration into the skin after topical application. In addition, unlike coenzyme Q10, idebenone protects against free radical formation and cell damage in conditions of hypoxic (low oxygen) cellular stress.³

Idebenone is relatively new to dermatology, and the standardized protocol just described has enabled it to be compared objectively with other popular topical antioxidants,

including L-ascorbic acid, DL- α tocopherol, kinetin, DL- α lipoic acid, and ubiquinone.

The results of the human sunburn cell assay showed that, among these antioxidants, idebenone had the greatest ability to reduce the development of sunburn cells after exposure to UV radiation—it resulted in a 38% lower sunburn cell count than in skin not treated with an antioxidant, compared with 30%, 20%, 11%, 9%, and 0% with tocopherol, kinetin, ubiquinone, lipoic acid, and ascorbic acid, respectively.¹

In terms of free radical scavenging activity, idebenone, ascorbic acid, and tocopherol showed the greatest activity (a concentration of 10 nmol/L was required for an antioxidant effect compared with 100 nmol/L with ubiquinone and ≥ 1000 nmol/L with kinetin and lipoic acid).

The greatest protection against lipid oxidation products was provided by kinetin and idebenone for primary oxidation products (lipid hydroperoxides reduced by 80% to 100% compared with 15% to 50% with the other antioxidants) and by lipoic acid and idebenone for secondary oxidation products (malondialdehyde equivalents reduced by 52% to 55% compared with 24% to 47% with the other antioxidants). Finally, the greatest inhibition of photoproduct generation in the nuclei of human keratinocytes was provided by idebenone (45%), followed by ascorbic acid and kinetin (36%), tocopherol (34%), ubiquinone (4%), and lipoic acid (0%).

Calculation of the Environmental Protection Factor showed that idebenone had the greatest antioxi-

Table 1. Environmental Protection Factor (EPF) calculated for idebenone, tocopherol, kinetin, ubiquinone, ascorbic acid, and lipoic acid.¹ For each of the five tests in the standardized protocol for assessing antioxidant activity, the agent showing the greatest activity was awarded the maximum score of 20 points. The other agents were awarded a percentage of this maximum score depending on the percentage of their activity in that test relative to the highest-ranking agent.

Evaluation	Idebenone	Tocopherol	Kinetin	Ubiquinone	Ascorbic Acid	Lipoic Acid
Sunburn cell assay	20	16	11	6	0	5
Free radical scavenging activity	20	20	10	15	20	5
Primary oxidative products	16	10	20	5	3	4
Secondary oxidative products	19	17	10	12	12	20
Ultraviolet B-irradiated keratinocytes	20	17	17	17	17	7
Total score (EPF)	95	80	68	55	52	41

dant activity overall, followed by tocopherol, kinetin, ubiquinone, ascorbic acid, and lipoic acid (Table 1).

Clinical Evaluation of Idebenone

A clinical evaluation of 1% idebenone in 21 female subjects with moderate photoaging showed that it also offers efficacy in reducing dyspigmentation and wrinkling.³ After twice-daily facial applications for 6 weeks, electrical conductance was used to assess skin hydration, and an expert grader assessed global improvement, fine lines and wrinkles, and skin roughness and dryness. At week 6, skin hydration was increased by 37%, and there was a 33% improvement in the global assessment of the skin's feel and appearance. Furthermore, there was a 29% reduction in the appearance

of fine lines and wrinkles and a 26% reduction in skin roughness and dryness. As a result, idebenone is the only antioxidant proven to help prevent sun damage to skin cells *and* to reduce fine lines and wrin-

“Idebenone is the only antioxidant proven to help prevent sun damage to skin cells and to reduce fine lines and wrinkles.”

kles. Photographic documentation demonstrates visible improvements in fine wrinkling (Figure 1) and dyspigmentation (Figure 2)—the ability of idebenone to improve dyspigmentation may relate to the fact that its structure is similar to that of hydro-

quinone. Idebenone was well tolerated with no irritation or adverse effects reported.

Topical Retinoids in the Treatment of Photodamage

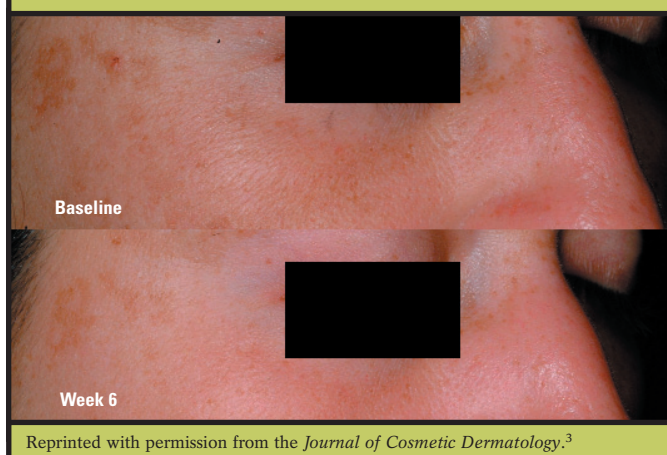
Topical retinoids have also demonstrated efficacy in reducing several manifestations of photodamage, including mottled hyperpigmentation, lentigines, irregular depigmentation, fine wrinkling, coarse wrinkling, elastosis, and tactile roughness.^{4,6} The US Food and Drug Administration has approved the 0.1% formulation of tazarotene cream and 0.02% and 0.05% formulations of tretinoin for the amelioration of certain signs of photodamage. In a 6-month study of 173 adults with fine wrinkling and mottled hyperpigmentation that com-

Figure 1. Improvement in fine wrinkling before and after twice-daily applications of idebenone 1% for 6 weeks.



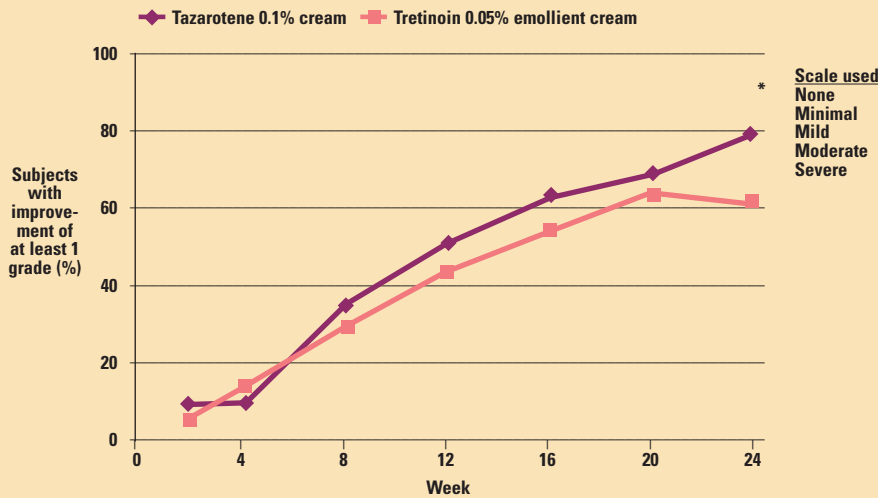
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Figure 2. Improvement in dyspigmentation before and after twice-daily applications of idebenone 1% for 6 weeks.



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Figure 3. Percentage of subjects showing an improvement in fine wrinkling of at least one grade (on a scale of none, minimal, mild, moderate, or severe) during treatment with tazarotene 0.1% cream or tretinoin 0.05% emollient cream.⁷



*P<0.01vs tazarotene emollient.

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“Idebenone is a particularly potent and effective antioxidant.”

pared tazarotene 0.1% cream with tretinoin 0.05% emollient cream, all significant between-group differences in efficacy measures were in favor of tazarotene.⁷ Tazarotene treatment was associated with a significantly higher percentage of patients achieving at least a one-grade improvement in mottled hyperpigmentation (at weeks 12 and 16) and fine wrinkling (at week 24) (Figure 3).⁷ (A one-grade improvement represents a change between grades of none, minimal, mild, moderate, and severe.)

Minimizing Aging of the Skin

Minimizing aging of the skin requires a combination of measures, including sun protection to minimize UV exposure, antioxidants to pro-

tect against oxidative stress, and topical retinoid therapy to ameliorate existing signs of photodamage. Sunscreens and potent antioxidants can provide excellent protection against further aging of the skin, and topical retinoids offer efficacy against existing signs of photodamage. Optimal results can be achieved by choosing the most effective product within each of these classes. Idebenone is a logical choice for antioxidant therapy as it is more potent than other commonly used antioxidants (ascorbic acid, tocopherol, kinetin, lipoic acid,

“Minimizing aging of the skin requires sun protection to minimize UV exposure, antioxidants to protect against oxidative stress, and topical retinoid therapy to ameliorate existing signs of photodamage.”

and ubiquinone) and is the only antioxidant proven to both help prevent sun damage to skin cells and reduce fine lines and wrinkles. Tazarotene cream is a logical choice for topical retinoid therapy as it is more effective than the only other retinoid indicated for the treatment of photodamage (tretinoin emollient cream).

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understood that topical retinoids act by helping prevent the development of microcomedones (the precursors of all acne lesions) and, as a result, are the cornerstone of therapy for both comedonal and inflammatory acne. It is this key ability to prevent the development of microcomedones that is also continuing to drive the evolution of topical retinoid therapy today. Given the ability to prevent both comedonal and inflammatory acne, topical retinoid therapy is the treatment of choice not only for initial therapy but also for maintenance therapy. Current research is demonstrating that, at least with tazarotene, maintenance therapy can achieve good results even in patients with moderate to severe inflammatory acne.¹¹

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recent consensus guidelines on treating acne,² which advocated the use of a topical retinoid plus an antibiotic/benzoyl peroxide product as a first-line therapy for comedonal acne. Study data support the use of clindamycin/benzoyl peroxide (although apparently not erythromycin/benzoyl peroxide) to enhance the anticomedonal efficacy of topical retinoid therapy.

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CME Posttest and Evaluation

Instructions: For each question or incomplete statement, one answer or completion is correct. Circle the most appropriate response. Seven correct responses are required for credit.

1. Which of the following medications has shown superior efficacy against all the others?
 - a. Tazarotene 0.1% gel
 - b. Adapalene 0.1% gel
 - c. Tretinoin 0.025% gel
 - d. Tretinoin 0.1% microsphere gel
2. What is the clinical significance of the ability of topical retinoids to prevent the development of microcomedones?
 - a. Optimizes efficacy against comedones alone
 - b. Optimizes efficacy against inflammatory lesions alone
 - c. Optimizes efficacy against both comedones and inflammatory lesions
 - d. Optimizes tolerability
3. The results of split-face studies show which of the following statements about the tolerability of topical retinoids to be true?
 - a. Adapalene cream is better tolerated than is adapalene gel.
 - b. Tazarotene cream is better tolerated than is tazarotene gel.
 - c. Tretinoin gel is better tolerated than tretinoin microsphere gel.
 - d. All of the above
4. Based on the clinical data presented, which of the following is the most rational choice to be used adjunctively with a topical retinoid as first-line treatment for comedonal acne?
 - a. Clindamycin
 - b. Minocycline
 - c. Clindamycin/benzoyl peroxide
 - d. Erythromycin/benzoyl peroxide
5. The adjunctive use of an appropriate topical antibacterial therapy with tazarotene can result in which of the following clinical benefits relative to tazarotene monotherapy?
 - a. Enhanced efficacy, no effect on speed of efficacy
 - b. Enhanced efficacy, deterioration in tolerability
 - c. Enhanced efficacy, enhanced speed of efficacy, enhanced tolerability
 - d. Enhanced efficacy, enhanced speed of efficacy, deterioration in tolerability
6. The results of the tazarotene/minocycline trial show that, with all three of the maintenance regimens, the percentage of patients sustaining at least a 50% global improvement from baseline after 12 weeks of initial therapy and 12 weeks of maintenance therapy was:
 - a. 60% to 70%
 - b. 70% to 80%
 - c. 80% to 90%
 - d. 90% to 100%
7. Which of the following may be valid reasons to use topical retinoid monotherapy as maintenance treatment for moderate to severe inflammatory acne?
 - a. Desire to minimize adverse effects associated with oral antibiotics
 - b. Desire to minimize the development of P. acnes resistance to antibiotics
 - c. Desire to avoid oral isotretinoin
 - d. All of the above
8. In a standardized protocol for assessing antioxidant activity, which of the following was found to have the greatest Environmental Protection Factor?
 - a. Ascorbic acid
 - b. Idebenone
 - c. Kinetin
 - d. Tocopherol
9. Which antioxidant has been proven not only to help prevent sun damage to skin cells but also to reduce fine lines and wrinkles?
 - a. Kinetin
 - b. Ascorbic acid
 - c. Idebenone
 - d. None of the above
10. During 24 weeks of treatment, tazarotene 0.1% cream has shown significantly superior efficacy to tretinoin 0.05% emollient cream for which of the following manifestations of photo-damage?
 - a. Mottled hyperpigmentation alone
 - b. Fine wrinkling alone
 - c. Both mottled hyperpigmentation and fine wrinkling
 - d. Neither mottled hyperpigmentation nor fine wrinkling

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