

# CLINICAL UPDATE

## Topical Retinoids in Acne: Emerging Strategies for Tolerability, Maintenance, and Skin of Color

**T**opical retinoids are a mainstay for the treatment of acne vulgaris, and several agents are currently available; however, key issues remain concerning the use of these agents. These issues include tolerability, optimal regimens for maintenance treatment, and use in skin of color. In addition, employment of antimicrobials for the management of acne has come under fire as a result of increasing rates of bacterial resistance. Each of these clinical considerations will be discussed in this supplement through a review of the literature, and practical tips to enhance patient outcomes will be provided.

### ACCREDITATION

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### TARGET AUDIENCE

This activity has been developed for dermatologists who are involved in the diagnosis and management of acne.

### EDUCATIONAL NEEDS

Although topical retinoids have been a mainstay in the treatment of acne, the strategies for their utilization continue to evolve. Emerging therapies and regimens offer dermatologists a broader range of options to improve tolerability, sustain positive clinical outcomes, and effectively treat a diverse patient population. This supplement provides an assessment of the current trends in topical retinoid therapy and discusses strategies for achieving the best results for patients with acne. Dermatologists reading this supplement can benefit from the practical tips and perspectives offered by the recognized program faculty and can apply this new knowledge in their daily practice to improve clinical outcomes for their patients.

### LEARNING OBJECTIVES

By reading and studying this supplement, participants should be able to:

- Identify practical and effective ways to improve tolerability of retinoids for the treatment of acne
- Understand and implement acne maintenance regimens for optimal clinical results
- Compare and contrast acne in patients with skin of color.

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**Dr Baldwin** serves on the Speaker's Bureau for Allergan Inc., Galderma Laboratories, OrthoNeurogena, and Stiefel Laboratories and is also a consultant for CollaGenex, Inc. **Dr Tanghetti** has received funding for clinical grants from, is a consultant for, and serves on the Speaker's Bureau for Allergan Inc. and Stiefel Laboratories. **Dr Taylor** has received funding for clinical grants from, is a consultant for, and serves on the Speaker's Bureau for Allergan Inc., Galderma Laboratories, and Johnson & Johnson Family of Companies. She intends to reference unlabeled/unapproved uses of tazarotene and tretinoin.

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## Improving Tolerability While Maintaining Efficacy: Practical Tips



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**T**he tolerability as well as efficacy of topical retinoids affect their clinical utility in acne vulgaris. The efficacy of topical retinoids is best judged one to another against comedonal acne. In data from a number of studies (N=630), reduction in comedonal lesion count after 12 weeks of therapy ranged from 55% to 71% for tazarotene 0.1% cream or gel and 36% to 48% for adapalene 0.1% cream or gel, tretinoin 0.025% gel, and tretinoin microsphere 0.1% (P values for tazarotene versus other agents ranged from  $P < 0.001$  to  $P = 0.042$ ) [*Cutis*. 2002;69(2 suppl):12-19; *J Drugs Dermatol*. 2005;4(2):153-158; *Cutis*. 2002;69(2 suppl):4-11; *Cutis*. 2001;67(6 suppl):4-9]. Thus, for comedonal acne, it is evident that more potent retinoids are more effective than less potent agents. Other clinical parameters, such as total lesion count and inflammatory lesions, may not adequately differentiate one retinoid from another, as all retinoids directly or indirectly reduce inflammatory lesion count. In the studies mentioned above, the reduction in inflammatory lesion

count showed less of a difference between agents and ranged from 54% to 70% for tazarotene preparations and 44% to 55% for tretinoin and adapalene (P values for tazarotene versus other agents significant only versus adapalene gel, where  $P = 0.0002$ ).

There are few studies addressing the comparative tolerability of retinoids. To address this issue, Leyden and colleagues utilized a split-faced, randomized, investigator-masked design in 253 healthy volunteers. Each subject used one retinoid formulation (tazarotene 0.05% and 0.1% cream, tazarotene 0.1% gel, adapalene 0.1% cream and gel, tretinoin 0.02% and 0.05% emollient cream, tretinoin 0.1% cream, tretinoin microsphere 0.1%) applied on one side of the face and a different formulation on the other side of the face for up to 29 days [*J Drugs Dermatol*. 2004;3(6):641-651]. Erythema and dryness/peeling varied between formulations and vehicles, and did not appear to be an attribute of any given retinoid. Skin sensitivity proved to be an important factor, with sensitive skin (history of difficulty with detergents or topical products) exhibiting worse tolerability than did normal skin (P values for dryness/peeling in those with normal versus sensitive skin ranged from  $P < 0.001$  to  $P = 0.059$ ).

In real-world clinical experience, all retinoids are inherently irritating, and patients with sensitive skin (ie, overreaction to all exogenous stimuli, and in conditions such as atopic dermatitis, rosacea, and psoriasis) typically find retinoids more irritating than do those with normal skin. A key challenge is to control irritation and thereby enhance tolerability. There are a number of factors that

can enhance the tolerability of all retinoids. More potent retinoids can then be used to permit the clinician to best address the patient's acne.

### Epidermal Barrier Integrity Is Linked to Tolerability

The problem with tolerability sometimes observed in patients with sensitive skin appears to be largely related to the integrity of the epidermal barrier. Epidermal barrier disruption leads to transepidermal water loss from the stratum corneum, with xerosis and peeling occurring when water content decreases below 10% [*Dermatol Clin*. 2000;18(4):597-607]. There are multiple forces besides skin sensitivity that work against efforts to maintain epidermal barrier integrity. These include products that contain soap and/or surfactants, or retinoids [*Br J Dermatol*. 1996;134(3):424-430], and environmental factors such as sunburn, low temperature, and low humidity.

There are some simple suggestions and solutions that can enhance the integrity of the epidermal barrier (Table 1). Indeed, barrier restoration alone may significantly improve outcomes in dermatologic conditions. Simple emollients play an important role in maintaining barrier function [*Am J Contact Dermat*. 2000;11(3):165-169; *Cutis*. 1998;61(6):344-346], with timing of application and type of product (hydrating versus occluding) being important considerations.

For example, a comparison of beta-methasone-17-valerate, hydrocortisone, and petrolatum for the treatment of

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# Skin of Color: Evaluating Similarities and Differences



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Clinical practice surveys in skin-of-color populations (individuals of African, Asian, Native American, and/or Latino descent) indicate that acne is among the top cutaneous disorders reported in these individuals, often ranking as the number one complaint. The chief concern among patients is not so much the acne lesion itself, but the resulting dark (hyperpigmented) macule, or postinflammatory hyperpigmentation (PIH) [*J Am Acad Dermatol.* 2002;46(2 suppl):S98-S106].

There are some racial differences in acne lesions. A survey of 1,646 incarcerated males showed the incidence of nodulocystic lesions to be lower in African American (0.5%) than in white (5%) subjects ( $P < 0.001$ ) [*Arch Dermatol.* 1970; 102(6):631-634]. (No conclusions were drawn from this study regarding Latino or Asian populations.) Histologic differences in acne have also been reported in African Americans, with biopsies of papular and pustular lesions demonstrating massive inflammatory infiltrates [*J Invest Dermatol.* 1996;106:888]. At least part of the mechanism underlying acne-induced PIH may involve production of the chemical mediators interleukin-1 alpha and prostaglandin  $E_2$  in keratinocytes as demonstrated following oleic acid (a fatty acid involved in acne) stimulation [*Pigment Cell Res.* 2003;16(5):603]. Acne-induced PIH can be long lasting, persisting for months or years, and can have devastating psychological effects.

Ideally, PIH should be prevented. Strategies include prompt treatment and prevention of acne,

avoidance of irritating medications, and sunscreen use. Sunscreen impacts the stimulatory effect of the sun on melanocytes as well as the transfer of existing melanosomes from melanocytes into keratinocytes. Patients should be encouraged to use sunscreen with both UVA and UVB protection such as the physical blockers (zinc oxide or titanium dioxide).

**Studies indicate that topical retinoids may offer a way to address both acne and PIH in those with skin of color.**

Hydroquinone (HQ)—which inhibits tyrosinase activity and the conversion of tyrosine to melanin—is currently the gold standard for treating PIH in the United States. However, it has no anti-acne activity, necessitating separate medications for the treatment of acne and PIH. In addition, possible regulatory changes (including a proposed US

Food and Drug Administration ban on over-the-counter HQ products and a New Drug Application requirement for all HQ-containing products) have the potential to severely limit HQ availability. Thus, there is a need for either new therapeutic options or a reassessment of existing options for the treatment of acne-related PIH.

## Topical Retinoids May Be Effective for PIH

Topical retinoids are currently a mainstay of acne therapy, and recent studies suggest they may be effective for the treatment of PIH as well. Topical retinoids are hormones that interact with nuclear retinoid receptors and regulate gene transcription. Their efficacy in acne derives from their ability to normalize desquamation of the follicular epithelium, promote drainage of comedones, and inhibit formation of new comedones [*Clin Ther.* 1992; 14(6):773-780; *J Am Acad Dermatol.* 1986;15(4, pt 2):907-915]. In addition, they appear to down-regulate gene expression dependent on AP-1 (a transcription factor associ-

ated with cell proliferation and inflammation), resulting in anti-inflammatory action.

The effectiveness of retinoids in the treatment of PIH is postulated to be related to inhibition of tyrosinase induction in melanocytes, enhancement of desquamation (which speeds up the sloughing of melanin in keratinocytes), inhibition of melanosome transfer from melanocytes to keratinocytes, and enhancement of the absorption of other ingredients.

The first study to demonstrate the efficacy of a retinoid in the treatment of PIH was reported by Bulengo-Ransby and colleagues in 1993 [*N Engl J Med.* 1993;328(20): 1438-1443]. In a randomized, double-blind study, 54 black patients with PIH received either vehicle or tretinoin 0.1% cream QD (along with daily sunscreen SPF 15 use) for 40 weeks. PIH was significantly lighter (as determined by investigator assessment) in tretinoin-treated than vehicle-treated subjects ( $P < 0.001$ ), with 91% of tretinoin patients judged as lighter or much lighter after treatment versus 57%

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## Improving Tolerability While Maintaining Efficacy: Practical Tips *continued from page 1*

irritant contact dermatitis showed petrolatum to be just as effective as betamethasone-17-valerate [*Exog Dermatol.* 2002;1(2):97-101].

### Improvements in Tolerability Are Seen With Combination Therapy

Combination therapy is increasingly being used for acne treatment. Two recent studies have examined the additive effects of an antibiotic/benzoyl peroxide (BP) product plus a topical retinoid and found that, contrary to an expected increase in irritation, the combinations were better tolerated than retinoid monotherapy.

A double-blind, randomized, parallel-group combination therapy study observed 121 subjects with moderate to severe acne treated with (1) a clindamycin 1%/BP 5% gel with humectants and occlusive agents QD AM plus tazarotene 0.1% cream QD PM or (2) vehicle gel QD AM plus tazarotene 0.1% cream QD PM [*J Drugs Dermatol.* 2006;5(3): 256-261]. Median percent change in open and closed comedo count was significantly better at all time points with the combination than with tazarotene alone (median reductions of 34% versus 18%, respectively, at week 4 and 70% versus 60%,

respectively, at week 12;  $P \leq 0.01$  for both comparisons). Median percent change in papule and pustule count was also greater with combination therapy than with tazarotene alone at weeks 8 and 12; this trend was most striking in those more severely affected at baseline (eg, with a median baseline papule/pustule count of  $\geq 25$ ), with median reductions of 63% (combination therapy) versus 52% (tazarotene alone) seen at week 12 in this subpopulation ( $P \leq 0.01$ ). Additionally, there was a lower overall incidence of peeling and dryness with the combination than with the single-agent regimen

(10% versus 18% and 8% versus 12%, respectively). Of particular interest, significant improvement in tolerability occurred during the first 4-week period of retinization.

The notion of improved efficacy and tolerability with combination retinoid therapy was repeated in a more recent study comparing adapalene 0.1% gel QD PM for 12 weeks with two other regimens: (1) clindamycin 1%/BP 5% gel (the same formulation used in the above-mentioned study) QD AM and adapalene 0.1% gel QD PM for 12 weeks and (2) clindamycin 1%/BP 5% gel QD AM for 4 weeks, then adapalene 0.1% gel added QD PM for the next 8 weeks [*J Drugs Dermatol.* 2007; in press]. The concurrent clindamycin/BP plus adapalene combination resulted in a significantly better reduction in inflammatory lesions ( $P < 0.05$ ) and nonsignificant reductions in noninflammatory and total lesion counts versus adapalene monotherapy. At week 4, dryness was significantly less with either combination than with adapalene monotherapy ( $P < 0.05$ ).

It is likely that the humectant and occlusive properties of the excipients in the clindamycin/BP product used in these studies contributed to

improved retinoid tolerability. Thus, when considering these types of combinations, consider the vehicle bases (water, alcohol, or emollient). These formulation characteristics can affect the overall tolerability of the regimen.

### Practical Strategies Can Enhance Tolerability

There are a number of practical strategies that can help minimize irritation when introducing a topical retinoid (Table 2). Consideration of anatomic variations can also decrease the chance of intolerance. For example, moisture can be a problem in some anatomic areas (eg, the perinasal region, oral commissures, lateral aspects of the chin). Conversely, retinoids are well tolerated periocularly and on the forehead, cheeks, and chin. Being aware of—and making allowances for—these anatomic differences can help patients optimize tolerance to these therapies.

Topical retinoids are a proven, effective option for the treatment of acne. Tolerability issues can be addressed in a number of ways, allowing us to confidently employ even the stronger and more efficacious of these therapies as an important part of our acne armamentarium. ■

**Table 1. Strategies for Maximizing Epidermal Barrier Integrity**

Variable	Impact	Solution
Soaps	Harsh soaps, especially alkaline products and products with powerful surfactants, remove protective lipids and damage the stratum corneum, which can result in increased absorption of topical retinoids and/or local irritation.	<ul style="list-style-type: none"> <li>Use non-soap cleansers.</li> <li>Wash gently with nonabrasive product.</li> </ul>
Water temperature	In addition to soap, hot water ( $>104^{\circ}\text{F}$ ) can damage the barrier function of the skin, resulting in permeability changes that also lead to increased absorption of topical retinoids and/or local irritation.	<ul style="list-style-type: none"> <li>Use warm (not hot) water for washing.</li> </ul>
Bathing	Long, hot showers and tub baths disrupt barrier function.	<ul style="list-style-type: none"> <li>Shorten bathing time.</li> <li>If dryness is an issue, consider applying an emollient immediately after bathing.</li> <li>Wait 20 to 30 minutes before applying retinoid to allow skin to normalize. Apply emollient to skin if necessary.</li> </ul>
Weather and humidity	Low-humidity environments (cold, dry weather; forced air heating; air conditioning; hot, dry weather) increase the sensitivity of the skin to barrier function disruption and can increase irritation from topical medications; high-humidity environments, on the other hand, are ideal for retinoids.	<ul style="list-style-type: none"> <li>Use moisturizer if dry.</li> <li>Use nonsoap cleansers.</li> <li>Consider retinoid holidays.</li> <li>Pay close attention to vehicles used.</li> </ul>
Emollients	Very important in maintaining and protecting the skin by restoring barrier function and reducing overabsorption of retinoids.	<ul style="list-style-type: none"> <li>Utilize an emollient prior to retinoid application where dry skin is/may be an issue; wait 15 to 30 minutes before applying retinoid.</li> </ul>
Astringents	Astringents can increase irritation from other topical medications by altering surface lipids and damaging the stratum corneum, causing overabsorption of retinoids.	<ul style="list-style-type: none"> <li>Eliminate astringents.</li> </ul>

**Table 2. Strategies for Minimizing Irritation During Retinization**

- Be pragmatic when initiating therapy.
  - Be especially careful during the first 4 to 6 weeks of therapy (retinization period).
- Consider combination therapy with a product that has humectant and occlusive agents.
- Consider using weaker-strength creams or gels during the first 4 to 6 weeks.
- Select retinoid formulation and vehicle best suited to seasonal temperature and humidity conditions.
- Consider alternate-day therapy during the first 1 to 2 months.
- Be open to other application methods (eg, short contact).
- Encourage the use of emollients to enhance barrier function of the skin.
- Educate patients about this period, and allow 1- to 3-day retinoid holidays.
- Consider a 1-month follow-up appointment after initiation of therapy.

# Maintenance Regimens for Acne: A Critical Assessment



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Acne is a chronic, relapsing condition that can have far-reaching psychosocial implications. Therapeutic improvement is only durable with isotretinoin therapy; thus, for those in whom isotretinoin is not indicated, maintenance therapy is a necessity. To optimize outcomes, efficacy, tolerability, and patient acceptability must all be considered when devising maintenance plans.

## Important Maintenance Therapy Strategies

Topical and/or oral antibiotics can be useful for initiating acne therapy but, because of bacterial resistance, should not be used as monotherapy or should be discontinued as soon as possible, ideally within 3 months. Since *Propionibacterium acnes* resistance was first observed in the early 1970s (soon after the introduction of topical erythromycin), an increasing prevalence of antibiotic-resistant strains has been reported [*Arch Dermatol.* 2003;139(4):467-471; *Br J Dermatol.* 2001;144(2):339-346]. By 1978, 20% of strains exhibited resistance; by 1996, resistance rates of up to 60% were observed. As a result, antibiotics are far less effective today against acne than previously. In addition, cross-resistance between clindamycin and erythromycin has reached 90% in some countries [*Br J Dermatol.* 2002;146(5):840-848; *Br J Dermatol.* 2001;144(2):339-346].

Concerns regarding antibiotic resistance go far beyond *P. acnes*, however. A much greater problem is the transfer of resistance to other types of bacteria, including those respon-

sible for upper respiratory infections (URIs) and/or methicillin-resistant *Staphylococcus aureus* (MRSA). In a study reported by Levy and colleagues (N=105) evaluating the long-term (>6 months) use of oral or topical antibiotics for acne, 85% of antibiotic-treated subjects cultured positive for tetracycline-resistant *Streptococcus pyogenes* in the throat versus 20% of those not receiving antibiotics ( $P=0.01$ ) [*Arch Dermatol.* 2003;139(4):467-471]. In a recently reported retrospective study (N=118,496), the odds for development of a URI in patients receiving  $\geq 6$  weeks of topical or systemic antibiotics for acne were 2.15 times greater than among those not receiving antibiotic treatment ( $P<0.001$ ) [*Arch Dermatol.* 2005;141(9):1132-1136]. The problem of MRSA has perhaps even more clinical significance. While in the United States most MRSA strains are still susceptible to tetracyclines, resistant strains are developing in Asia [*Clin Infect Dis.* 2006;42(3):389-391; *Jpn J Infect Dis.* 2004;57(2):74-77]. As tetracyclines are our least expensive and safest oral agent for treating MRSA, maintaining their antimicrobial activity needs to be a priority.

Antibiotic resistance can be avoided by adding benzoyl peroxide (BP) to acne regimens. The addition of BP not only can improve response to antibiotic therapy, but also, obviates or even reverses antibiotic resistance among *P. acnes* [*Am J Clin Dermatol.* 2004;5(4):261-265; *Clin Ther.* 2002;24(7):1117-1133].

## Influences on Patient Compliance

Another important component to maintenance therapy is the careful choice of the vehicle via which active compounds are delivered. Simply put, medications that are not used do not work, so if a patient has an aversion to the selected vehicle type, compliance may become an issue. Vehicle choice may, in fact, be the most important decision we make when designing a maintenance therapy regimen. It is a decision that should be made with the patient since a reduction in side effects, improvement in compliance, and the resulting improved efficacy are often seen when patients are empowered by having a say in which vehicle is utilized.

Another factor in medication compliance is dosing frequency. In terms of enhancing compliance, decreasing the number of products seems to be more important than decreasing dosing frequency, and combination creams may be helpful when trying to minimize the number of products used.

## Maintenance Plans Should Be Individualized

In acne maintenance, there is no "one size fits all" plan; instead, maintenance therapy regimens must be tailored to the individual. In addition to vehicle choice, patients' willingness to tolerate some side effects, their lifestyle preferences, and their efficacy goals (eg, is "better" okay, or do they want and need "clear") should all be considered.

How dramatically patients can differ in these regards is illustrated by what is generally seen in teenaged patients versus adult female patients. Teenagers are often willing to accept an improvement in acne severity, while women are rarely willing to accept anything less than "clear." In teenagers, compliance is often poor, and the concept of delayed gratification can be beyond their grasp. Thus, cycling is common. In contrast, in women, compliance is often better, and there is generally an understanding that today's actions bring tomorrow's benefits. In both groups, the duration of therapy necessary for maintenance is daunting ("until you are 18" seems like forever to teenagers, as does the need to continue therapy until menopause in women).

Because of the inherent differences seen between these groups, maintenance regimens for each also often differ. In teenagers, it is generally wise to utilize the fewest medications possible to accomplish an acceptable level of efficacy. In addition, teenagers will not use medications that are irritating and their treatment cannot be visible to the outside world. Last, treatment must be self-applicable (a teenage boy is not going to ask for help applying a medication to the back). Women, on the other hand, are generally willing to use more products to accomplish their goal of "clear"; they are also more willing to accept minimal irritation. In addition, the

need for an ongoing maintenance regimen can often be made more palatable in this population by touting the dual anti-aging and anti-acne benefits of retinoid therapy.

## Multiple Maintenance Therapy Options Exist

Recommended maintenance therapy options are presented in the Table. Topping this list are retinoid therapies, as studies have shown these agents can be efficacious as monotherapy against both non-inflammatory and inflammatory acne. Maintenance therapy utilizing a retinoid plus an antibiotic has also been explored in some recent studies, as treatment with this combination has been shown to result in faster, more complete clearance.

In the first of these studies, 189 patients received minocycline 100 mg BID plus tazarotene 0.1% gel QD PM for 12 weeks; those with  $\geq 75\%$  improvement (as determined by investigator assessment) were then randomized to receive minocycline or tazarotene or both for an additional 12-week period [*Arch Dermatol.* 2006;142(5):605-612]. No significant efficacy differences were seen between groups in the maintenance phase; however, there were trends towards better maintenance of improvements with the antibiotic-containing regimens, especially against inflammatory lesions (Figure).

In a similar study, 253 patients successfully treated (ie, those showing at least moderate improvement from baseline on a 6-point scale) with 12 weeks of adapalene/doxycycline combination therapy were randomized to receive 16 weeks of adapalene 0.1% gel or placebo gel QD [*Arch Dermatol.* 2006;142(5):597-602]. At the end of the treatment period, maintenance of improvement was seen in 75% versus 54% of those treated with adapalene versus placebo, respectively ( $P<0.001$ ); lesion counts were also significantly lower in adapalene- versus placebo-treated patients ( $P=0.005$ ).

Because of these trends towards superior efficacy with topical retinoid/antibiotic combination therapy, another suggested maintenance therapy option is the utilization of a topical

### Table. Maintenance Therapy Options for the Treatment of Acne

- Topical retinoids alone
- Topical retinoids + BP
- Anti-inflammatory—dose doxycycline
- Hormonal therapy
- Low-dose isotretinoin

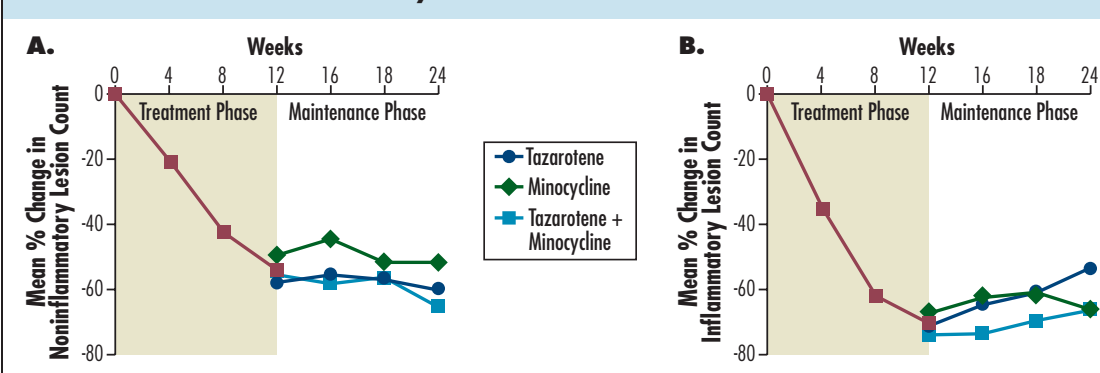
retinoid plus a BP product, as BP may offer an alternative to antibiotics by avoiding the risk of bacterial resistance.

Another choice for maintenance therapy is anti-inflammatory—dose doxycycline. In a study reported by Parish and colleagues (N=12), doxycycline hyclate 100 mg QD was administered for 8 weeks, after which those exhibiting a  $\geq 50\%$  improvement qualified for an 8-week maintenance study during which they were randomized to receive doxycycline hyclate 20 mg BID (a dose associated with mean plasma concentrations that remain below the antimicrobial threshold) or placebo [*Acta Dermatovenerol Croat.* 2005;13(3):156-159]. Those receiving doxycycline maintained their improvements (as measured by mean change in lesion count versus baseline); those receiving placebo did not.

A final option for maintenance therapy is low-dose isotretinoin. This is a highly efficacious maintenance option in those for whom it is indicated. There are, however, safety issues associated with long-term use (teratogenicity and night blindness), and isotretinoin is most appropriately prescribed to male patients and female patients of non-childbearing potential.

Maintenance is an integral component of most acne treatment plans. Indeed, to ignore the need for maintenance therapy is to guarantee failure in the majority of patients. Safe and effective options exist; a plan that matches these options to individual needs and desires has the best chance of producing successful and satisfying results. ■

**Figure. Mean Change in Noninflammatory (A) and Inflammatory (B) Lesion Counts in Patients Treated With Minocycline or Tazarotene or Both**



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**Skin of Color: Evaluating Similarities and Differences** *continued from page 2*

with vehicle. Improvement was noted after 4 weeks and persisted throughout the study. Colorimetry analysis confirmed investigator assessments, showing a 40% versus 18% lightening of lesions toward normal skin color in tretinoin- versus vehicle-treated subjects ( $P=0.05$ ). No patients receiving tretinoin worsened with treatment.

Another, more recent study evaluated tazarotene for the treatment of PIH [*Cutis*. 2006;77(1):45-50]. In this study, 74 patients with skin of color with mild to moderate

facial acne and acne-induced PIH were randomized to receive double-blind tazarotene 0.1% cream or vehicle QD for up to 18 weeks.

Compared with vehicle, tazarotene was more effective (as determined by investigator assessment) in lessening overall PIH severity ( $P=0.010$ ) and in reducing the pigimentary intensity ( $P=0.044$ ) and area ( $P=0.026$ ) of the hyperpigmented lesions. Erythema, burning, and peeling were trace or less, and dryness was mild or less throughout the study in both treatment groups.

The effectiveness of tazarotene in the treatment of PIH has also been observed in African American and Hispanic patients with pseudo-folliculitis barbae (PFB) [Poster presented at: American Academy of Dermatology ACADEMY '02; July 31-August 4, 2002; New York, New York]. In this investigator-masked, split-faced, placebo-controlled, parallel-group study, 50 patients with PFB related to shaving applied tazarotene 0.05% or 0.1% gel to the beard area on one side of the face and vehicle to the other side QD for 90 days.

Following treatment, significantly greater reductions were seen with tazarotene than with placebo in the overall severity of PFB ( $P\leq 0.001$  with tazarotene 0.05% gel and  $P\leq 0.05$  with tazarotene 0.1% gel at day 60) and PIH ( $P\leq 0.05$  for both tazarotene products at day 60). Peeling, itching, burning, dryness, and tingling were experienced in 26% and 43% of sites treated with tazarotene 0.05% and 0.1% gel, respectively; the majority of these adverse events were mild and resolved spontaneously.

These studies indicate that topical retinoids may offer a way to address both acne and PIH in patients with skin of color, thereby maximizing convenience and, likely, patient satisfaction. There is a need for additional studies in wider segments of the skin-of-color population (including those of Asian and Latino descent), as such studies will help us better understand and treat acne and related concerns in darker skin. ■

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**Topical Retinoids in Acne: Emerging Strategies for Tolerability, Maintenance, and Skin of Color**

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**CME INSTRUCTIONS:** For each question or incomplete statement, choose the answer or completion that is correct. Circle the most appropriate response. Three of five correct responses are required for credit.

- Which of the following is NOT recommended as a strategy for maximizing epidermal barrier integrity?
  - Use of nonsoap cleansers
  - Use of warm water instead of hot water for washing
  - Use of an emollient
  - Use of an astringent
- Recent studies have found that combination acne therapy involving an antibiotic/benzoyl peroxide product with emollient plus a topical retinoid is:
  - Associated with increased efficacy, but also an increase in irritation
  - Better tolerated than retinoid monotherapy
  - Better tolerated than retinoid monotherapy, except during the period of retinization
  - None of the above
- Which of the following statements regarding antibiotic therapy for acne is true?
  - The addition of benzoyl peroxide to acne maintenance regimens can prevent or even reverse antibiotic resistance.
  - Oral—but not topical—antibiotic therapy for acne should be discontinued as soon as possible, ideally within 3 months.
  - A recent study showed that significantly more subjects receiving short-term (<3 months) oral or topical antibiotic therapy for acne cultured positive for tetracycline-resistant *Streptococcus pyogenes* in the throat versus those not receiving antibiotics.
  - When evaluating maintenance therapy, improvements in efficacy have not been seen with antibiotic/topical retinoid combination therapy versus topical retinoids alone.
- Which of the following are variables that need to be considered when devising an acne maintenance therapy regimen for an individual patient?
  - Vehicle preference, efficacy goals, and whether or not an antibiotic was used as initial acne therapy
  - Vehicle preference, ability to tolerate side effects, and whether or not an antibiotic was used as initial acne therapy
  - Ability to tolerate side effects, efficacy goals, and whether or not an antibiotic was used as initial acne therapy
  - Vehicle preference, ability to tolerate side effects, and efficacy goals
- Which of the following statements regarding acne-induced postinflammatory hyperpigmentation (PIH) is true?
  - Concerns about acne-induced PIH are generally secondary to concerns about the acne lesions themselves in those with skin of color.
  - At least part of the mechanism underlying acne-induced PIH may involve suppression of the chemical mediators interleukin-1 alpha and prostaglandin E<sub>2</sub> in keratinocytes.
  - Sunscreen utilization is a key component in the prevention of PIH.
  - Although topical retinoids are effective against acne, studies investigating the efficacy of these compounds in PIH have been disappointing.

**COURSE EVALUATION**

Please Print (All information is confidential.)

Name: \_\_\_\_\_ Specialty: \_\_\_\_\_

Degree:  MD  DO  Other \_\_\_\_\_

Affiliation: \_\_\_\_\_

Address: \_\_\_\_\_

City: \_\_\_\_\_ State: \_\_\_\_\_ ZIP: \_\_\_\_\_

Telephone: \_\_\_\_\_ Fax: \_\_\_\_\_

E-mail: \_\_\_\_\_ Signature: \_\_\_\_\_

**CME CREDIT VERIFICATION**

I verify that I have spent \_\_\_\_\_ hour(s)/\_\_\_\_\_ minutes of actual time working on this CME activity. No more than 1 CME credit will be issued for this activity.

**PRETEST ASSESSMENT:** Please rate your prior knowledge of topical retinoids in acne on a scale of 1 to 5, with 1 being the lowest and 5 the highest. 1 2 3 4 5

**COURSE EVALUATION:** Please evaluate the effectiveness of this activity by circling your choice on a scale of 1 to 5, with 1 being the lowest and 5 the highest.

**Objective #1:** Identify practical and effective ways to improve tolerability of retinoids for the treatment of acne 1 2 3 4 5

**Objective #2:** Understand and implement acne maintenance regimens for optimal clinical results 1 2 3 4 5

**Objective #3:** Compare and contrast acne in patients with skin of color 1 2 3 4 5

1. How do you rate the overall quality of the activity? 1 2 3 4 5

2. How do you rate the educational content of the activity? 1 2 3 4 5

3. After participation in this activity, have you decided to change one or more aspects in the treatment of your patients?  Yes  No

If yes, what change(s) will you make? \_\_\_\_\_

If no, why not? \_\_\_\_\_

4. Was the presented information fair, objective, balanced, and free of bias in the discussion of any commercial product or service?  Yes  No

If no, please comment: \_\_\_\_\_

5. Suggested topics for future activities: \_\_\_\_\_

6. Suggested authors for future activities: \_\_\_\_\_

7. Would you be willing to participate in postactivity follow-up surveys?  Yes  No

8. Would you be willing to participate in a phone, e-mail, or in-person discussion exploring ways to improve our CME activities?  Yes  No

*The EOCME thanks you for your participation in this CME activity. All information provided improves the scope and purpose of our programs and your patients' care.*