Therapeutic Advances in the Topical Management of Acne

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- Formulation Advancements
- Topical Therapy Overview
- Gender Response and Adult Acne
- Enhancing Retinoid Tolerability
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Therapeutic Advances in the Topical Management of Acne

Acne is one of the top diagnoses dermatologists make in practice. And yet, despite its omnipresence and the wealth of data that has bolstered understanding of its pathogenesis and treatment, acne remains a therapeutic challenge. The needs of individual patients often demand specific and varied interventions. Fortunately, clinicians have access to an array of treatment options among which is an ever-growing arsenal of topical agents; topical therapy remains the cornerstone of effective acne care for most patients. As new data continue to elucidate the pathophysiological components of acne, strategies to optimize the efficacy of existing therapies, and the subtleties of barrier function and repair, it is incumbent upon clinicians to identify the unique needs of each patient and match it with an efficacious regimen.

NEW AVENUES IN FORMULATIONS
There are established algorithms and guidelines that direct the topical treatment of acne in most cases. Specifically, Andrea Zaenglein, MD notes that these guidelines call for the initiation of treatment for topical therapy candidates with an antimicrobial and a retinoid. In the case of retinoids, she says that patients very often are steered toward generic formulations by their insurance carriers, and these formulations may tend to be more irritating than branded formulations. Writing for a specific formulation, such as tretinoin gel microspheres (Retin-A Micro, Valeant Dermatology) or tretinoin gel 0.05% (Atralin, Valeant Dermatology), may improve tolerability, she suggests. The availability of coupons and rebates has been very helpful, Dr. Zaenglein says, making it easier to give patients access to prescription therapies their insurance may not cover.

**Benzoyl Peroxide.** Benzoyl peroxide (BPO) remains one of the most prominent acne therapies available. Patients treated with systemic or topical antibiotics should always undergo concomitant topical therapy with a benzoyl peroxide-containing product, a strategy shown to reduce the development of bacterial resistance, Joseph Bikowski, MD reminds. “In addition, a topical retinoid is of primary value in acne management and may be used in conjunction with a systemic antibiotic,” he adds.

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**TABLE. DIFFERENTIAL DIAGNOSIS OF ACNE VULGARIS**

The differential diagnosis of acne includes several common “red face” diseases that clinicians should keep in mind.

**Rosacea.** Rosacea (sometimes called “acne rosacea,” though this technically inaccurate term has fallen out of widespread use) typically affects adults, with earliest onset usually reported in the early-to-mid 20s. Open and closed comedones are not seen in rosacea, although papules/pustules may be seen.

**Perioral dermatitis.** More common in women than men, the pathogenesis of perioral dermatitis is not well understood. In fact, perioral dermatitis is often used as an imprecise descriptor for any eruption of unknown origin affecting the perioral area. Allergic contact dermatitis may be implicated, as may misuse of topical corticosteroids.

**Drug-induced folliculitis.** A manifestation of a systemic drug reaction, monomorphic lesions can form on the head, upper trunk, and proximal upper extremities. Commonly implicated drugs include: corticosteroids, androgens, ACTH, lithium, isoniazid (INH), and phenytoin.

**Pseudofolliculitis barbae (PFB).** As a result of shaving, hair shafts may perforate below the skin surface and become trapped, leading to the formation of inflammatory papules.

—Joseph Bikowski, MD

(Continued on page 8)
It’s important to recall the rationale for topical therapy, its occasional limitations, and its potential to benefit a majority of acne patients.

BY JOSEPH BIKOWSKI, MD

A majority of patients with mild-to-moderate acne will be managed quite adequately with topical therapy alone. We know there are four main pathogenic factors in acne:

- Increased androgen secretion
- Increased sebum production
- P. acnes proliferation
- Faulty keratinization.

Currently, no topical therapy is available to modulate androgen levels or androgen receptors at the follicular level, nor are there topical therapies that can modulate sebum production. However, topical therapies are available to:

- Regulate keratinization
- Decrease P. acnes colonization
- Inhibit associated inflammation.

### An Overview of Topical Acne Therapy

<table>
<thead>
<tr>
<th>TOPICAL THERAPIES AND THEIR ACTIONS</th>
<th>Anti-comedonal</th>
<th>Anti-P. Acnes</th>
<th>Anti-inflammatory</th>
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<td>Tretinoin</td>
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<td>- Generics</td>
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<td>- Retin-A Micro Pump 0.04%, 0.1%</td>
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<td>- Tretin-X 0.01%, 0.025%, 0.05%, 0.1%</td>
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<td>Adapalene</td>
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<td>- Differin Gel 0.1%, 0.3% (Galderma)</td>
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<td>Tazarotene</td>
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<td>- Fabior Foam 0.1% (Stiefel)</td>
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<td>Benzoyl peroxide</td>
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<td>- Cleocin T 1% (Pfizer)</td>
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<td>- Akne-ycin 2% (Valeant Dermatology)</td>
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<td>- Evoclin 1% (Stiefel)</td>
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<td>- ClindaReach 1% (DUSA)</td>
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<td>Clindamycin/benzoyl peroxide</td>
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<td>- Duac Gel, CLI 1%/BPO 5% (Stiefel)</td>
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<td>Dapsone</td>
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<td>Adapalene/BPO</td>
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<td>- Epiduo 0.1%/25% (Galderma)</td>
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<td>- Ziana, CLI 1.2%/tretinoin 0.025% (Medicis)</td>
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<td>- Veltin CLI 1.2%/tretinoin 0.025% (Stiefel/GSK)</td>
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+++ Signifies primary effect
+ Signifies secondary effect
- Signifies no effect
? Signifies undetermined effect
Topical retinoids primarily function to regulate hyperkeratinization, preventing the formation of microcomedones and encouraging resolution of clinically apparent comedones. They also confer anti-inflammatory effects (i.e., reducing and preventing erythematous papules and pustules).1-5

Despite treatment guidelines indicating that topical retinoids—tretinoin, adapalene, tazarotene (See table)—are appropriate for use in a majority of patients with mild-to-moderate acne,6,7 data suggest topical retinoids may be underutilized.8,9

Several topical antibacterials and antimicrobials have been shown to decrease or eradicate P. acnes. Topical benzoyl peroxide has demonstrated activity against P. acnes, and has the benefit of not being associated with promoting antibacterial resistance. Concentration-dependent irritation has been noted, however, data show that 2.5% and 5% concentrations confer similar efficacy to 10% benzoyl peroxide.10 Benzoyl peroxide is also shown to confer comedolytic and keratolytic effects.11

Topical antibiotics (clindamycin or erythromycin) also confer activity against P. acnes and have demonstrated anti-inflammatory effects.12 Their use as monotherapy has largely diminished given the substantial body of data showing that use of benzoyl peroxide in combination with a topical antibiotic confers greater efficacy, enhances tolerability compared to either agent alone, and obviates concerns about developing resistance.11

Several fixed-combination formulations are available that feature benzoyl peroxide along with clindamycin. A novel combination of benzoyl peroxide and adapalene is available for once-daily use in the management of acne vulgaris. In trials, adapalene/benzoyl peroxide fixed-dose combination gel was more effective than either component as monotherapy, with safety similar to that of each component and vehicle.13

Topical dapsone, a relative newcomer to the market, is the first primarily anti-inflammatory topical treatment for acne. Analysis of pooled data from three studies involving 1,306 patients age 12 to 15 found that dapsone gel was safe and effective when used for up to 12 months.14

Optimal treatment of acne depends on the initiation of therapy aimed at multiple pathogenic features of the disease, and the majority of patients with mild-to-moderate acne are best treated with a combination of topical therapies.6,7,15 Given the importance of topical retinoids in the management of acne and their ability to prevent the formation of the early microcomedo, most patients should be started on a topical retinoid each evening. Treatment is optimized with the addition of a topical antimicrobial, either topical benzoyl peroxide or benzoyl peroxide/antibiotic combination, each morning. In the case of fixed combination adapalene/benzoyl peroxide, it is indicated for once-daily application. ■

Clinicians should consider a number of factors when selecting a benzoyl peroxide product. Among these are formulation, vehicle tolerability, and concentration. Regarding tolerability, Emil Tanghetti, MD notes that while it may be unrealistic to expect no irritation at all, reducing irritation while maintaining efficacy is the ultimate goal of treatment. "Benzoyl peroxide is an oxidizing molecule and therefore is inherently irritating. The idea is to deliver enough of it to be effective and not too much to be irritating," Dr. Tanghetti suggests. Integral to improving a formulation’s irritation profile is the addition of excipients, such as humectants and/or emollients, he says. For example, "The combination clindamycin phosphate and benzoyl peroxide 1.2%/5% (Duac, Stiefel/GSK) includes both a humectant and an emollient, which helps to reduce irritation," says Dr. Tanghetti.

Other means of reducing irritation include using lower concentrations of BPO. "Lower percentages, like 2.5% BPO, seem to work as well as higher percentages and are associated with less irritation," explains Julie C. Harper, MD. Formulations such as the combination adapalene and benzoyl peroxide 2.5% (Epiduo, Galderma) offer lesser amounts of BPO with comparable efficacy.

"The 'more is better' concept is not necessarily true anymore," observes Joshua Zeichner, MD. "With innovation in vehicle formulation and drug delivery, some products with lower concentrations of benzoyl peroxide are delivering equivalent drug levels to products with higher BPO concentrations," he explains.

Lower concentration may also help mitigate irritation. "Benzoyl peroxides can certainly be irritating, but this appears to be dose dependent in many individuals, with lower doses associated with less irritation," says Dr. Harper. This has been seen in many topically applied products, Dr. Harper observes. "For example, higher concentrations of topical retinoids seem to be more irritating than lower concentrations," she says. The unique advantage of adapalene/benzoyl peroxide 2.5% is that efficacy doesn’t appear to change despite the decreased concentration of BPO.

**Solubilized and Micronized BPO.** Another approach to improving BPO tolerability has been the introduction of solubilized BPO. Unsolubilized BPO tends to be a large molecule that will essentially "sit" on the skin, where it can produce irritation and may not be readily delivered to the target. The literature has offered varying results on the potential benefits of solubilized BPOs. However, Dr. Tanghetti points to one study that examined solubilized 5% benzoyl peroxide (CLENZIderm M.D., Obagi), as compared to generic clindamycin/benzoyl peroxide and found that the solubilized 5% BPO worked more rapidly over the first few weeks. 1 “Results were similar at the end of the month, nevertheless the rapid onset of action is notable,” Dr. Tanghetti notes. “Solubilized BPO can also have a rather profound effect on comedones, which probably has something to do with the excipients as well as the BPO,” observes Dr. Tanghetti.

Another attempt to improve the tolerability and availability of BPO is micronization. BPO is milled to a consistent small size that allows for deeper penetration and reduces clumping. One product featuring micronized BPO is OTC Effaclar Duo (BPO 5.5% plus lipohydroxy acid [LHA], La Roche-Posay). In a recently published double-blind study, treatment with OTC Effaclar Duo BID plus tretinoin 0.025% QPM was as effective at 12 weeks as clindamycin 1%–BPO 5% BID plus tretinoin 0.025% QPM. 2

"This over-the-counter product with benzoyl peroxide and lipohydroxy acid offers another option to combine with prescription medications, like topical retinoids," Dr. Zeichner observes. “In this study, the efficacy of this OTC product with

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**PERCEPTIONS OF TEENAGE ACNE**

A recent study explored the perception of teenage acne among both teens and adults. Survey participants were asked a series of questions of teens shown in photographs with and without acne (via digital photo manipulation). There was no mention of acne in the questions or the survey invitation.

Results showed that teens and adults (percentages reported respectively) perceived teenagers with acne as:

- shy (39 percent, 43 percent)
- nerdy (31 percent, 21 percent)
- stressed (24 percent, 20 percent)
- lonely (23 percent, 22 percent)
- boring (15 percent, six percent)
- unkempt (13 percent, seven percent)
- unhealthy (12 percent, eight percent)
- introverted (nine percent, 23 percent)
- rebellious (seven percent, five percent).

In a companion survey of teens with acne, respondents reported:

- embarrassed (64 percent)
- lower self-confidence or shyness (71 percent)
- difficulty finding dates (43 percent)
- problems making friends (24 percent)
- challenges with school (21 percent)
- trouble getting a job (seven percent).

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tretinoin was comparable to that of a benzoyl peroxide/antibiotic combination with tretinoin. These results are promising and give dermatologists confidence in recommending this particular OTC product to treat their acne patients.

**Combination Products.** As suggested above, combination products can be used to great benefit, Dr. Zeichner notes. Combination products such as clindamycin and BPO 1%/5% gel (Benzaclin, Sanofi-Aventis), adapalene/BPO, or tretinoin/clindamycin (Ziana, Medicis), are especially helpful when the physician is looking to simplify the regimen, Dr. Zaenglein says. In addition, dermatologists now understand that BPO can be used in combination with tretinoin microspheres, as the spheres protect the tretinoin from degradation. This allows for the creation of a once-a-day, simplified regimen. Microspheres offer another potential benefit: there is evidence that use of tretinoin gel microspheres or specially formulated topical products, like Galderma’s DermaControl oil control product, can reduce surface oiliness “without stripping the skin of natural oils,” Dr. Zaenglein says. This can be a plus for patients with oily skin or those concerned about surface “shine.”

Dr. Tanghetti observes that there are unique challenges to using combination products. This is especially true with topical retinoids, which fundamentally change barrier function and are inherently irritating: “When you are using retinoids in combination with clindamycin/benzoyl peroxide, you want to avoid agents that will be irritating. Benzamycin, for example, is a BPO with an alcoholic base and is inherently more irritating.” Therefore, Dr. Tanghetti recommends water-based formulations, or products with humectants and emollients, which are better tolerated when creating an irritating environment on the skin.

Fixed-dose combinations allow patients to get the benefit of more than one agent in a single application. According to Dr. Zeichner, multiple types of combinations exist to fit the patient need and physician preference. These combinations include BPO/clindamycin, BPO/retinoid, and retinoid/clindamycin. According to Dr. Tanghetti, the individual ingredients of a fixed combination product may not be particularly effective against acne by themselves, but the combination with others provides improved efficacy. For example, when using clindamycin as a monotherapy, resistance will often develop rather rapidly and compromise the efficacy of clindamycin, suggests Dr. Tanghetti. “However, if you use clindamycin concurrently in combination with benzoyl peroxide 2.5% (Acanya, Valeant Dermatology) over 16 weeks, the combination prevents resistance and as a consequence you’re likely to get better efficacy,” explains Dr. Tanghetti. Resistance is less of an issue with adapalene/benzoyl peroxide 2.5%, and the BPO does complement the action of the topical retinoid very nicely, remarks Dr. Tanghetti. “They both work in different ways and yet they each do many of the same things,” he says. Studies suggest that the two agents work synergistically, meaning that the sum of two agents’ combined action is greater than the sum of the efficacy of the constituent parts.

In addition, Dr. Tanghetti remarks, BPO has an antibacterial effect that retinoids do not, whereas both BPO and clindamycin have complementary antibacterial properties. The possibilities for combination therapy in topical acne management are wide-ranging. Thus, according to Dr. Zeichner, the ideal acne regimen takes advantage of combination therapy, though not always fixed-dose combinations. “If one ingredient is not included in the combination product, it can be added to the regimen as a single agent,” explains Dr. Zeichner. Fixed-dose products sometimes have limitations. “The main limitation is that they only come in fixed concentrations, and if you want a higher concentration of one of the ingredients, then you will need to change the product,” says Dr. Zeichner. Additionally, topical dapsone (Aczone, Allergan), which has shown to be an effective alternative to BPO, is only available as a monotherapy product, Dr. Zeichner explains. “Unfortunately, the perfect topical combination drug containing all the ingredients in one product does not exist,” he says.

With the variety of topical formulations available—from solubilized BPO to fixed combinations—it is important to understand that efficacy can range considerably, notes Dr. Tanghetti. Moreover, the lack of head-to-head trials in many of the approved agents is limiting. “We now know the importance of the formulation and how the active ingredient is delivered into the skin, but it remains difficult to know whether a certain concentration of BPO is more effective or less irritating than another,” says Dr. Tanghetti. Ultimately, it comes down to how the formulation is delivered. “If an agent is delivering the drug more efficiently, one might anticipate more irritation, but given the lack of head-to-head Phase IV trials, it is difficult to know,” he says. Thus, clinicians must gain familiarity with each of these agents to make specific recommendations for their patients, particularly when it comes to BPOs. In addition,
it’s worth noting that formulations of benzoyl peroxide alone are only sold over the counter, Dr. Zaenglein says. This makes it important that dermatologists “know about the available options and be prepared to make specific product recommendations if they choose to recommend benzoyl peroxide alone,” she says.

**Foams.** Topical foam formulations have become increasingly popular in dermatology over the last several years, with potential benefits in terms of patient tolerability, convenience, and adherence. The newest foam approved for acne treatment is tazarotene 0.1% foam (Fabior, Stiefel/GSK).

Foams may be especially useful for treatment of large surface areas of hair-bearing skin. Back and chest acne are estimated to occur in 61 percent and 45 percent of acne patients, respectively. In one study, half of patients with facial acne were found to also have truncal involvement, while three percent of patients had only truncal involvement. There is, surprisingly, some evidence that patients with truncal acne may not recognize that they have truncal involvement, suggesting that clinicians should be more attentive to truncal acne and specifically question patients about any evidence of acne on the chest, shoulders, or back.

“Treatment of trunk acne, particularly on the back, is notoriously challenging,” Dr. Bikowski observes. Attempts to make treatment easier and hopefully improve compliance have included novel application systems, such as ClindaReach (DUSA Pharmaceuticals), and easy-to-spread formulations, like clindamycin phosphate foam 1% (Evoclin, Stiefel). “In clinical studies, clindamycin foam was superior to clindamycin gel or the foam vehicle for reducing total, inflammatory, and non-inflammatory acne lesion counts,” according to Dr. Bikowski.

A new benzoyl peroxide emollient foam wash formulation has shown efficacy against trunk acne when used as a short-contact therapy. “BenzFoam Ultra (BPO 9.8%, Onset Dermatologics) significantly reduced P. acnes counts when it was used in a short-contact protocol,” Dr. Bikowski says. “Patients should be instructed to apply BPO 9.8% foam to the dry back before showering once daily and leave it in place for two minutes. When they get in the shower, they should simply rinse the formulation off and wipe the treated area with a wet cloth.”

The short-contact protocol is convenient and relatively easy to perform, Dr. Bikowski says. The data suggest that the BPO foam wash can be used as monotherapy, especially for maintenance of clearing. For most patients, “It’s a good option to use in combination with topical clindamycin or even oral antibiotics to reduce the risk for developing resistance.”

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**GENDER RESPONSE AND ADULT ACNE**

An emerging area of interest in acne research and therapy is treating adult acne, particularly acne in women over 20. In terms of age distribution of acne, Dr. Harper notes that males may have more acne in the teenage years, but females take over in the adult years. “Overall, we believe the pathogenesis of acne is the same at all ages and therefore the basic treatment algorithm is very similar,” explains Dr. Harper. “Adults may not be as oily as teenagers with acne, so prescribing well-tolerated products is crucial. Additionally, visible peeling and dryness that can sometimes accompany acne treatments are not acceptable to many of our adult patients,” she says. That’s why she emphasizes the importance of involving all patients in the development of a treatment plan, especially adults. “They expect to be educated about their condition and need to be given options when discussing their treatment plan with a physician,” says Dr. Harper.

The apparent gender differences in the presentation of acne and response to therapy are vexing. “Around the age of 20, we start to see a shift in the distribution of acne,” notes Dr. Tanghetti. “Approximately 25 percent of adult women have acne and it appears to be a different kind of acne, to some extent,” says Dr. Tanghetti. Noting an increased presentation of acne in the perioral area in adult women, Dr. Tanghetti says that this type of acne can scar easily and become a persistent problem for women. Additionally, adult women tend to break out more along the lower one-third of the face and neck, says Dr. Zeichner. “While a comedonal subtype does exist, in my practice, I mainly see inflammatory papules. This type of acne is likely different from the acne teenagers get, but we need more research to evaluate this type of acne,” says Dr. Zeichner.

Dr. Tanghetti explains that women’s sebaceous glands—stimulated by androgens—tend to flare during periods...
of hormonal fluctuation. Thus, hormonal therapies are particularly well-suited to this group. These include oral contraceptive pills and spironolactone. Currently, there are four oral contraceptives with a specific indication for acne: Beyaz (Bayer Healthcare), Yaz (Bayer Healthcare), Ortho Tricyclen (Janssen), and Estrostep (Warner Chilcott).

Aside from oral contraceptives, Dr. Harper notes that topical dapsone has been shown to have anti-inflammatory effects and superior efficacy in female patients. “We have always believed that the pathogenesis of teenage and adult acne is basically the same, but it doesn’t look the same clinically. The distribution is different and the primary visible lesion is different,” notes Dr. Harper. “The fact that it may respond differently to treatment, therefore, is not surprising,” she continues. Dr. Tanghetti points to a study that evaluated more than 3,000 patients receiving topical dapsone and showed a very clear gender difference in response to therapy.6 “Women fared much better with both active drug and vehicle than men,” says Dr. Tanghetti. “It didn’t seem to be based on a compliance issue, but instead on gender, which probably has a pathophysiological basis since this is largely hormonally driven,” he explains. In particular, data increasingly suggest that the sebaceous glands are central, according to Dr. Tanghetti. “We have learned that the sebaceous glands are tied to the production of oil and sebum, and various inflammatory factors, as well. Thus, the sebaceous glands function almost like a neuro-endocrinological gland, if you will, and are very important in the scope of what we know about acne,” says Dr. Tanghetti. “We still have much to learn about those glands and how gender affects our acne therapeutic protocols,” he adds.

Aside from demonstrating the benefits of topical dapsone and the importance of the sebaceous glands, the topical dapsone data underscore the need for clinicians to think more critically about developing therapies that address the specificities of each patient group. Dr. Harper emphasizes the need for more data looking at the potential gender difference in acne and response to treatment. Moreover, she is hopeful that deeper inquiry will turn out improved understanding of these differences. “I think we are on the cusp of learning a great deal about what causes adult female acne,” she says. In turn, this data may carve out new understandings for acne in general.

A special consideration for treatment of adult women is the challenge of acne in pregnancy. Therapy must be administered with caution, as even many topical agents are not demonstrated to be safe for use by pregnant women. Dr. Bikowski notes that azelaic acid (AzA) is a treatment option that may be worth considering for pregnant women who desire a treatment. “Azelaic acid is a saturated dicarboxylic acid found naturally in wheat, rye, and barley. Azelaic acid is present in foods and has no known fetal effects. It is rated Category B,” Dr. Bikowski explains. “Its antimicrobial, anti-inflammatory, and antikeratinizing properties are beneficial for acne management. I tend to prescribe the 15% gel formulation (Finacea, Intendis), which is not indicated for acne therapy in the US, but which has a favorable tolerability profile.”

The prevalence of adult women with acne will hopefully provide clinicians with more than an enhanced understanding of the disease, Dr. Tanghetti observes. “Women with acne are understandably frustrated with us as providers. Thus, as a field, we need to do better communicating with them and understanding how to design our acne treatments for each group and each patient,” Dr. Tanghetti explains.

ADHERENCE AND COMMUNICATION

As research continues to turn out fresh ways to think about and approach the topical treatment of acne, clinicians will likely continue to work against forces such as misinformation and non-compliance. “It used to be that the doctor was the patient’s primary source of medical information. Today the Internet is,” Dr. Zaenglein observes. Despite the clinician’s best efforts to educate patients and correct misinformation, patients will likely continue to encounter false information online, including promises of quick cures. Dialogue, patience, and persistence are critical, she says.

An equally important issue that can pose roadblocks to effective care is non-compliance. On the therapeutic level, Dr. Zeichner advises several strategies for boosting compliance. “Simple regimens improve compliance. A fixed-dose combination product applied once per day, for example, can give better results and better adherence than applying the same ingredients separately twice per day,” says Dr. Zeichner. But while tweaking the treatment regimen may provide some benefit, patient education is perhaps the most essential component in improving compliance, according to Dr. Harper. In addition to knowing how much medicine to use and when to use it, Dr. Harper explains (Continued on page 17)
Tips for Optimizing Retinoid Tolerability

With these considerations in mind, prescribers may support a more comfortable treatment experience for patients.

BY DIANE HANNA, ARNP-C AND TRACY CLARK, ARNP-C

APPLICATION. Historically, it has been a widely accepted practice to apply retinoids at night time. In a clinical study sponsored by OrthoDermatologics, oily skinned patients using micronized or microspheres containing formulations had a reduction in shine with the introduction of QAM application. Therefore, clinicians are now rethinking application schedules.

Traditionally the standard application amount is referred to as a pea-size amount. Because of the relationship between dosage and irritation, application amount is key. However, in the pivotal trials each retinoid had its own dosage regimen. See Table 1 for dosing as indicated in each PI.

VEHICLE SELECTION. There are many different vehicle choices for retinoids. Oily skin patients are more likely to be able to withstand an alcohol-based gel (note, though, that many gels are now water-based), whereas more sensitive-skinned patients tend to fair better with cream formulations. However, patients may have preferences for a particular vehicle, and it may be worthwhile to question patients prior to choosing a therapy.

MOISTURIZERS. Another common practice is the introduction of moisturizer to help manage cutaneous symptoms. No pharmacodynamics, placebo-controlled, safety, and efficacy studies have been done to understand the impact on co-application or mixing of moisturizers with topical retinoids. Still, it is a widely accepted practice. One approach is to apply the moisturizer prior to the application of topical retinoids. The application of a physical barrier is thought to slow down the penetration and absorption of the molecule and decrease irritation. A commonly reported approach is to mix the topical retinoid with a moisturizer, again for the purpose of the creation of a barrier to slow down absorption. Some clinicians instruct patients not to combine moisturizer with their medication and encourage frequent use of moisturizer as desired throughout the day.

In the winter months, in areas of the country where humidity drops, the skin naturally becomes dry. Moisturizers that focus on barrier repair, such as Restoraderm or Cetaphil (Galderma), and CeraVe (Valeant), are useful in protecting the skin from the elements and managing side effects. These specific moisturizers are non-greasy, noncomedogenic and contain lipids and ceramides that keep moisture and essential fats in the skin.

“Clinicians are well aware that patients have limited capacity to absorb and retain information given in a 10-minute office visit.”

Educate patients to anticipate irritation and help them understand it signifies a response to therapy.

Choose formulations optimized for slow absorption of the retinoid, which decreases irritation.

Advocate use of moisturizers.

Titrate the application/dose, if needed.

Choose the best vehicle for the patient’s skin type and preference.

Provide handouts.

BASIC STRATEGIES FOR INCREASED TOLERABILITY, BETTER ADHERENCE

- Educate patients to anticipate irritation and help them understand it signifies a response to therapy.
- Choose formulations optimized for slow absorption of the retinoid, which decreases irritation.
- Advocate use of moisturizers.
- Titrate the application/dose, if needed.
- Choose the best vehicle for the patient’s skin type and preference.
- Provide handouts.
PATIENT HANDBATS. Clinicians are well aware that patients have limited capacity to absorb and retain information given in a 10-minute office visit. Written clarification is a helpful tool, and many brand-specific handouts are available to providers.

Having a simple office-based handout that mimics the provider’s generalized treatment approach is helpful in reinforcing the message. Key points to include are:

1. Expected time for global improvement
2. Application time (am or pm)
3. Dosing schedule (daily, every other day, etc.)
4. Recommended moisturizers and how to apply them
5. What to do if irritation occurs (call office, decrease dosing).


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that patients should know why they are being given two or three prescriptions to treat their acne. “Explaining the role of each agent certainly improves adherence,” says Dr. Harper. Setting appropriate expectations for treatment and involving the patient in developing the treatment plan is also crucial, she stresses. “We must discuss tolerability, safety, and potential risks, but also costs,” she says, noting that patient preference for treatment should be a major consideration.

Regarding side effects of topical therapy, Dr. Harper suggests that all patients should be briefed on what to do when side effects occur. “Many of our topical products may cause some dryness and/or peeling within the first few weeks of treatment,” says Dr. Harper. “If patients don’t know that this is normal, they will simply give up.” Instead, patients should understand that some side effects will occur early.

Also important in the scope of education, according to Dr. Zeichner, is counseling patients on the importance of skin care and which OTC products to use. Advise against harsh cleansers and especially scrubs—“they only create micro tears in the skin,” Dr. Zenglein says. Use of a moisturizing sunscreen is also essential. Dr. Zeichner adds that if a patient is on an irritating medication, daily use of a moisturizer can help with the irritation.

Patient education is one of the defining elements of successful acne therapy, and it cannot happen without a sound foundation of communication. “Communicating well with our patients is hugely important when it comes to fostering a trusting relationship,” says Dr. Harper. As in any relationship, becoming a good listener may be the most important part of communicating well, Dr. Harper observes. As for other specific techniques for improving communication with patients, Dr. Harper emphasizes the importance of making good eye contact with the patient. Moreover, Dr. Tanghetti advises that you address the patient—not the parents—no matter how young the patient. “Often the patient sits there and Mom or Dad does the talking, but that’s not an ideal way to get adherence,” says Dr. Tanghetti. “You have to speak to them directly and ask, ‘What works for you?’ ‘What’s your typically routine like?’ ‘What do you do?’ ‘When do you shower?’ ‘Do you wash your face?’ ‘Do you brush your teeth twice a day?’” Dr. Tanghetti explains that asking these questions not only helps your relationship with the patient but can also allow the patient to tie their treatment to some kind of habitual behavior.

Also a factor in sound communication with patients is finding out what they have used in the past, notes Dr. Zeichner. “If something did not work, find out why. Maybe they used too much and got irritated. Maybe they did not use it long enough, which is why they did not get a result,” Dr. Zeichner suggests.

A trusting relationship with the patient is a most significant aspect of treatment, according to Dr. Tanghetti, because it will allow the clinician to set expectations for treatment. Once you establish a good interaction with the patient, says Dr. Tanghetti, “you can facilitate a program that’s better suited to the patient,” rather than opting for a one-size-fits-all approach. But none of this can occur if the right expectations are not in place, he reminds. “The hard part is telling acne patients that they will not see much improvement for eight weeks, however, it is critical to set this expectation.” If you don’t do this and a patient fails to see results in two weeks, it is likely that you will lose them, Dr. Tanghetti observes. That is why taking the small amount of time required to establish a trusting relationship with a patient—i.e., making good eye contact, listening to his or her concerns, etc.—is ultimately what will gain success in treatment, says Dr. Tanghetti.

**CONCLUSION**

Recent developments on both the research and therapeutic fronts suggest a bright future for acne care. While the latest data on gender response to treatment in adult patients suggests that much is still yet to be learned about the pathophysiology of acne, it has also further opened the door to a more nuanced approach to understanding and treating the disease. As more new agents and molecules enter development and become available, clinicians are seeing their treatment toolboxes continue to expand. Given the varied response to existing treatments that researchers and practicing clinicians have observed, it has become clear that not all acne is created equal and that each patient requires a personalized approach. This coupled with an emphasis on communications allow clinicians to find the right treatment that all patients deserve.

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DISCUSS POTENTIAL SIDE EFFECTS

Dr. Harper: It is important to discuss what to do when side effects do occur. Many of our topical products may cause some dryness and/or peeling within the first few weeks of treatment. If patients don’t know that that is normal, they will simply give up. Explain that early side effects can occur. Bless a few days off of treatment here and there—instead of quitting all together.

Dr. Zaenglein: Ask patients to call if they have any problems...We can discuss ways to improve tolerability.

ADDRESS SKIN CARE

Dr. Harper: Talk about skin care and the use of moisturizers.

Dr. Zeichner: Combine irritating products with moisturizers to help reduce irritation.

SET REALISTIC EXPECTATIONS

Dr. Zaenglein: Explain up front that this will take a while to work, probably six to eight weeks... Most often, irritation from the commonly used acne formulations is mild and transient, and it peaks at about two weeks.

REINFORCE THE HABIT

Dr. Zaenglein: I recommend putting the acne medication right next to the toothpaste on the sink rather than away in a medicine cabinet. This way, the patient is going to stare at those products at least twice a day while brushing their teeth.

CONSIDER PREFERENCES

Dr. Zeichner: Ask patients what their preferences are. When do they want to put on medicines: evening or morning? Do they prefer a wash?

KNOW THE TREATMENT HISTORY

Dr. Zeichner: Find out what patients used in the past. If something did not work find out why. Maybe they used too much and got irritated. Maybe they did not use it long enough, which is why they did not get a result.

REDUCE THE LIKELIHOOD FOR CONFUSION

Dr. Zeichner: Give out written instructions.

PREEMPT THE INTERNET EFFECT

Dr. Zaenglein: Talk about the information that is out there on the Internet up front.