Given that 40 to 50 million people in the US are affected by acne vulgaris, dermatologists are comfortable with its management and familiar with the range of available topical and systemic treatment options. Yet familiarity with the condition can lead clinicians to overlook new treatment options or emerging evidence about acne and the experiences of affected patients.

Because current evidence suggests that acne is a result of increased sebum production and follicular hyperkeratinization compounded by host responses to the proinflammatory activities of Propionibacterium acnes, combination therapy targeting the multiple components of acne is commonplace. Studies have documented multiple benefits associated with various combination therapies, including the superiority of combinations to constituent parts alone as well as improved convenience for patients and, subsequently, better compliance. Among popular topical combination therapies are fixed combination formulations of clindamycin and benzoyl peroxide, including the recently approved formulation Acanya (clindamycin-BPO 2.5%, Arcutis).

Familiar Agents
Benzoyl peroxide (BPO) has been a mainstay of topical acne management for years. It is safe and effective for treating acne. Its efficacy is maintained over many years of use with the distinct advantage of not being associated with antimicrobial resistance. In addition, BPO has anticomedogenic and keratolytic properties.

The primary limitation of BPO has been concentration-dependent cutaneous irritation and dryness that develops in certain patients. Furthermore, a small subset of patients can also have...

Rediscovering Topical Antimicrobial Therapy for Acne Vulgaris

The number of potential topical therapy combinations for management of acne vulgaris can be astounding. Specific characteristics of the patient’s clinical presentation determine treatment selection.

By Joseph Bikowski, MD
Therapies in Practice

**Table 1. Acne Grading for the Clinician**

A meaningful acne grading system should convey in a clear manner the: type, number, and location of lesions. Choose a descriptor from each of the first two columns to describe acne in each affected anatomic area. For example, a patient may have grade I mild acne of the forehead and both cheeks and grade II and III moderate acne of the back.

<table>
<thead>
<tr>
<th>Grade (Type)</th>
<th>Severity (Number)</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I - Comedo</td>
<td>Mild disease: 1-10 lesions</td>
<td>Forehead</td>
</tr>
<tr>
<td>Grade II - Papule</td>
<td>Moderate disease: 11-20 lesions</td>
<td>Cheeks (Right, Left, both)</td>
</tr>
<tr>
<td>Grade III - Pustule</td>
<td>Severe disease: &gt;20 lesions</td>
<td>Nose</td>
</tr>
<tr>
<td>Grade IV - Nodulocyst</td>
<td></td>
<td>Chin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shoulders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest</td>
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<td>Back</td>
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</table>

allergic contact dermatitis in response to BPO. Of note, the frequency and severity of burning, erythema, and peeling associated with BPO was significantly greater in patients who used topical formulations containing concentrations of 10% compared with those who used a 2.5% concentration. Studies show that BPO concentrations of 2.5% may be as effective as 5% or 10% concentrations in reducing the number of inflammatory lesions of acne and significantly reduce *P. acnes* counts after one week of topical application to the face. As a result, it is generally recommended to initiate treatment with a low concentration of BPO to minimize local side effects.

Clindamycin phosphate offers direct activity against *P. acnes*. Furthermore, it has been shown to decrease inflammation and tetracyclines are more popular for oral use. Among topical antibiotics, clindamycin appears to offer better efficacy than erythromycin. Clinicians have favored topical antibiotic agents when appropriate for the treatment of acne in efforts to minimize systemic antibiotic exposure.

Fixed combination products of clindamycin 1% and benzoyl peroxide 5% are widely accepted and used for the treatment of acne. Many studies have shown that the combination of clindamycin 1% with BPO 5% is superior to each individual active ingredient. It has also been suggested that a once-daily treatment for acne that is effective and has minimal irritation may contribute to improved patient compliance.

Understanding their Role

In my practice, I “grade” acne according to a previously described system that identifies the type (comedo, papule, pustule, and nodular-cyst), number, and location of lesions (See Table 1). Based on trials and clinical experience, it is now generally accepted that retinoids are most effective for comedones (Grade I). They have been shown to provide anti-inflammatory effects, as well. Topical antibacterials or systemic antibiotics best treat papules and pustules (Grades II and III). Nodulocystic acne (Grade IV) typically requires systemic antibiotics or oral isotretinoin. As such, fixed combination antibiotic/benzoyl peroxide formulations alone may be appropriate for patients with primarily papular or pustular acne of mild to moderate severity. Topical combination antimicrobial formulations may be used in conjunction with topical retinoids when comedones are present.

Expanding Options

A new fixed-dose, once-daily combination gel containing clindamycin phosphate 1.2% (equivalent to 1% clindamycin) and a low concentration of BPO (Acanya) is now available and provides a worthwhile treatment option for a range of acne presentations.

In two identical Phase III studies involving 2,813 patients with moderate to severe inflammatory and non-inflammatory acne Acanya showed statistically superior efficacy over active ingredients and vehicle for both inflammatory and noninflammatory lesions. After 12 weeks of treatment, mean inflammatory lesions were reduced by over 54 percent with the combination agent and noninflammatory lesions by 43 percent, compared to only 29 percent and 24 percent with vehicle, respectively (p<0.001). Over one-third of treated subjects (35 percent) were judged to be “treatment successes” by investigators (at least a two-grade improvement in global severity by the Evaluator Global Severity Score (EGSS)), compared to 16.5 percent of controls (p<0.001). Just over a quarter (29 percent) of treated patients were determined to be “clear/almost clear” at Week 12, compared to 12.7 percent of controls (p<0.001) (Table 2). Importantly, patients were satisfied with the results of therapy, which was well tolerated. Using the Subject Self Assessment (SSA) scale, almost 40 percent of subjects judged their acne to be “clear/almost clear” at Week 12 with superior improvements to vehicle evident as early as Week 2. Reported mean Patient Satisfaction Scores (PSS) on a 10-point scale (10 being most satisfied)
were significantly greater at Week 12 (7.5) compared with their prior acne therapy (4.2) (p<0.001).

The incidence of adverse drug reactions was low and similar across all treatment groups (the majority ≥97 percent were ‘mild to moderate in severity’). Application site reactions with Acanya were rare (0.1 percent) and only one patient discontinued Acanya due to application site pain and irritation. Local signs and symptoms were minimal for all patients and no patient discontinues treatment because of these (Table 3).13

**Vehicles Drive Therapy**

Attention has focused on the role of vehicles in enhancing tolerability of therapy and thereby improving patient satisfaction and compliance. In addition to the concentration of active ingredients, such as BPO or retinoids, other components of the vehicle, such as surfactants or alcohol, can also cause skin irritation.17,18 Aqueous gel formulations have become popular in dermatology because they offer easy application and cosmetic elegance without the drying and irritating effects of alcohol, which formed the basis of some early gel formulations.

As previously noted, I emphasize the site of involvement when classifying acne because it impacts the treatment approach. Whereas topical creams may be suitable for the face, they may not be suited to application to a hairy chest or back. Gels, by contrast, may be more easily applied to hair-bearing skin, such as the beard area, chest, shoulders, and back. Patients may prefer gels for oily facial skin and men may prefer gels for facial application. However, when a choice of vehicle exists, it is worthwhile to question patients about their specific preferences and previous treatment experience prior to selecting therapy.

Of course, the primary function of the vehicle is to drive the active ingredient into the skin. Data show that in vitro percutaneous absorption of BPO in human skin (measured as benzoic acid) from Acanya was comparable to that with commercially available fixed combination preparations containing BPO 5%. Clinical studies to compare the efficacy of Acanya to that of fixed combination products containing 5% concentrations of BPO, have not been conducted at this time.20

**Involve the Patient**

When they present to the dermatologist for treatment of acne, most patients will have already tried either over-the-counter or prescription therapies to manage their condition. Benzoyl peroxide is the mainstay of OTC acne therapy. Dermatologists who prescribe BPO-containing combination products to their patients with Grade II to III mild to moderate acne may encounter some resistance, either because previous BPO therapy failed or resulted in irritation and dryness. Explain the additive effects of fixed

![Mean Percent Reduction in Lesion Count (Week 12)](chart.png)
combination formulations compared to their constituent parts. It is essential that clinicians take time to discuss therapy selection with patients. Explain that topical antimicrobial agents most effectively target the inflammatory component of acne and discuss the need for a topical retinoid, if indicated, to address comedones and provide further efficacy for papules and pustules.

Explain that higher concentrations of active ingredients do not necessarily offer greater efficacy. A 21-day cumulative irritation study of various concentrations of BPO found that lowering the concentration of BPO from 5% to 2.5% produced a 33 percent reduction in mean cumulative irritation score; further lowering the concentration to 1% had little additional effect. The irritation seen with 5% BPO concentrations was lower than that seen in other studies comparing skin irritation with fixed combination products containing 5% BPO, although direct comparisons are not possible due to different study designs.

Address the role of vehicle in efficient therapy delivery. Choose vehicles suitable to the application site and that meet the patient’s preferences. Finally, when available, choose once-daily product formulations over more frequently applied products in order to enhance compliance.

Dr. Bikowski has served on the advisory board, served as a consultant, received honoraria, and/or served on the speaker’s bureau for Allergan, Barrier, CollaGenex, Coria, Galderma, Intendis, Medicis, OrthoNeutrogena, PharmaDerm, Quinnova, Ranbaxy, Sanofi-Aventis, SkinMedica, Stiefel, UCB, and Warner Chilcott.

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