

The Diagnosis and Management of Mild to Moderate Pediatric Acne Vulgaris

Successful management of acne vulgaris requires a comprehensive approach to patient care.

By Joseph B. Bikowski, MD

As a chronic, inflammatory skin disorder affecting susceptible pilosebaceous units of the face, neck, shoulders, and upper trunk, acne presents unique challenges for patients and clinicians. Characterized by both non-inflammatory and inflammatory lesions, three types of acne have been identified: neonatal acne, infantile acne, and acne vulgaris; pediatric acne vulgaris is the focus of this article. Successful management of mild to moderate acne vulgaris requires a comprehensive approach to patient care that emphasizes 1.) education, 2.) proper skin care, and 3.) targeted therapy aimed at the underlying pathogenic factors that contribute to acne. Early initiation of effective therapy is essential to minimize the emotional impact of acne on a patient, improve clinical outcomes, and prevent long-term sequelae, such as scarring.^{1,2}

Part I: Acne Vulgaris Diagnosis

Epidemiology and Pathogenesis

Acne is estimated to affect 85 percent of the population in the US. While females are more likely to

seek treatment, males tend to have more severe presentations. Acne typically begins between seven and 10 years of age and peaks between the ages of 16-19 years. A majority of patients clear by 20-25 years of age, however some patients continue to have acne beyond 40 years of age. So-called "adult acne," persisting beyond the early-to-mid 20s, is more common in women than in men. Given the hormonal mediators involved, acne onset correlates better with pubertal age than with chronological age.

Take-Home Tips. Successful management of mild to moderate acne vulgaris requires a comprehensive approach to patient care that emphasizes 1.) education, 2.) proper skin care, and 3.) targeted therapy aimed at underlying pathogenic factors that contribute to acne. Given the importance of topical retinoids in acne management and their ability to prevent microcomedos, most patients should be started on a topical retinoid. Treatment is optimized with the addition of a topical antimicrobial. 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. ●

Four pathogenic factors contribute to acne. Elevation of dehydroepiandrosterone (DHEA-S) levels associated with puberty is generally considered an inciting event. Increased DHEA-S promotes increased sebum production, which in turn encourages the proliferation of *Propionibacterium acnes*, a commensal organism normally found on the skin. Concurrently, abnormal keratinization of the follicular canal occurs with subsequent blockage of the follicle and build-up of sebum

A combination of sebum and keratinocytes collects in the follicle, leading to the formation first of a clinically undetectable microcomedo and then of clinically apparent open or closed comedones (whiteheads and blackheads).³ In the case of the closed comedo (whitehead), the follicle swells with keratinous and sebaceous debris, but the follicular opening remains constricted and is covered over by epidermis. In the open comedo (blackhead), the follicular orifice widens as the follicle swells, but a dark-colored mixture of keratinocytes, oxidized lipids, and melanin forms a plug in this opening.

The material that collects in the comedo also contains the inflammatory by-products of *P. acnes*, which is shown to induce antimicrobial peptide and proinflammatory cytokine/chemokine expression.⁴ However, since the material remains contained in the follicular unit, an inflammatory host response is not initiated. If the contents spill out of the follicle into the surrounding tissues of the dermis, an inflammatory response is initiated, leading to the formation of inflammatory papules and pustules. In severe acne, nodules may form.

Acne is not caused by dirt, grease, grime, oil on the skin, chocolate, soft drinks, nuts, pizza or any other dietary components.⁵ Recent research attempt-

Types of Acne Lesions

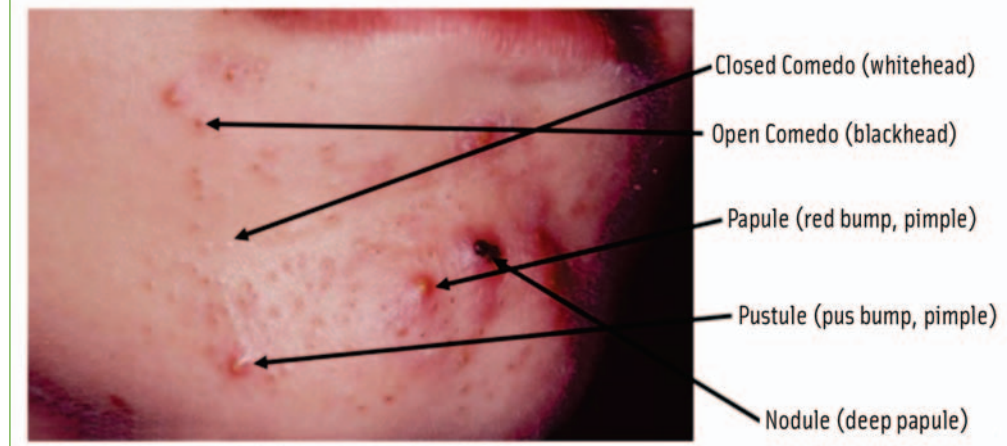


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ing to elucidate a causative link between diet and acne has failed to definitively identify a relationship, though some evidence suggests that diet can influence the course of acne. Specifically, high glycemic load diets have been associated with exacerbation of acne, and there is scant evidence implicating dairy foods in the worsening of acne.⁶

Acne is a chronic disease that can be characterized by periods of exacerbations and remission, but generally it is not classified as a progressive disease.¹ Left untreated, a patient with mild disease at age 10 will likely have mild disease at age 15, while a patient with untreated severe disease at an early age will likely have severe disease later in adolescence.

Though not fully elucidated, hereditary influence in acne has been identified; if both parents had severe acne then the offspring has a high risk for severe acne. Studies show that a family history of acne is associated with earlier onset of acne and recalcitrance.⁷

Acne Assessment

While several different acne grading scales have been used in clinical trials, no standard method for acne grading has been adopted into practice. The Basic Acne Severity Index is a proposed method for assessing acne severity based upon lesion type, number, and location.¹¹

Type of lesion. The lesion type is designated by a grade. Since there are four primary lesion types, there are four grades from I to IV. Importantly, these grades simply describe a lesion morphology and are not intended to represent a qualitative severity "ranking." For example, a Grade I lesion is no more or less severe than a Grade IV lesion.

Grade I - comedo

Grade II - papule

Grade III - pustule

Grade IV - nodulo-cyst

Number of lesions. One to 10 lesions constitutes mild acne. Moderate acne is 11 to 20 lesions. More than 20 lesions is severe.

Location of lesions. Typical anatomic sites of involvement include:

Head

- Face
 - Forehead
 - Cheeks – Right or Left
 - Nose
 - Chin
- Ears

Neck

Torso

- Shoulders
- Chest
- Back

When Laboratory Testing and Referral Are Indicated

While elevated androgen levels are implicated in the pathogenesis of acne vulgaris, in relatively rare instances androgen excess associated with systemic diseases may contribute to atypical acne presentations: early onset, severe presentation,⁸ or treatment resistance. Simple laboratory tests aid diagnosis, though comprehensive specialist evaluation is indicated. Clinicians should be aware of these potential diagnoses that may manifest with severe or treatment resistant acne:

1. Delayed onset congenital adrenal hyperplasia.⁹
2. Adrenal or ovarian tumor.¹⁰
3. Cushing's disease.¹⁰
4. Polycystic ovary syndrome.¹⁰

Acne Impact and Sequelae

Acne vulgaris can have a strong psychosocial impact on affected patients,¹² with one studying showing that mental health scores among affected adults were worse than those for patients with asthma, epilepsy, diabetes, back pain, arthritis, and coronary artery disease.¹³ In surveys of affected teens and adults acne has been shown to lead to decreased dating, sports, and eating out, impaired academic performance, and increased unemployment rates.¹⁴

Post-inflammatory hyperpigmentation (PIH) or persistent darkening of the skin in areas of healed acne lesions can occur in patients of all skin types, though it is more common in patients of color.¹⁵⁻¹⁷ PIH results from the deposition of melanin at the site of previous inflammation and may persist indefinitely without treatment. Post-inflammatory erythema, by contrast, is reddening at the site of involvement that resolves over time.

Differential Diagnosis for Adolescent Acne

The differential diagnosis of acne vulgaris includes several "red face" diseases.

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), 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.

Scarring is a common sequelae of acne,^{18,19} and the risk may be increased among patients who “pick” and “pop” lesions, causing trauma to the follicular unit and surrounding structures.

Early initiation of therapy is expected to minimize the development of damaging sequelae.^{1,2} Of note, particular therapeutic agents, such as topical retinoids (discussed below) can be useful to treat acne vulgaris as well as post-inflammatory hyperpigmentation.¹⁵⁻¹⁷

Part II: Comprehensive Management of Mild to Moderate Pediatric Acne Vulgaris

Effective management of acne vulgaris requires a comprehensive approach to patient management that depends on three critical elements: patient education, good basic skin care, and appropriate therapy.

Patient Education

Inform patients that although acne cannot be cured (i.e., taken away so that it never comes back), it certainly can be controlled. Setting appropriate expectations is important, including how long it will take treatment to take effect and the likely duration of treatment. Note that the typical patient may anticipate just six months of treatment or less.¹² Treatment must be used on a consistent basis, despite a common perception among teens that acne is a transient disease.²⁰ Initial results from therapies can be expected in about four to six weeks. To achieve best results with any regimen will require eight to 16 weeks.

Advise patients to discontinue all over-the-counter skincare programs and therapies: No soaps, astringents, cleansers, fresheners, toners, scrubs, facial masks or cosmetic skin care programs. Given that only a relatively small proportion of the estimated population affected by acne



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Figs 1-3. Post Inflammatory Erythema (top), Post Inflammatory Hyperpigmentation (middle), acne scarring (bottom).

seeks treatment from a physician, it seems reasonable to assume that a majority of patients have tried over-the-counter therapies.²¹ Had non-prescription remedies provided benefit, the patient would not be in the office, therefore, he or she should be willing to abandon those therapies.

Dispel common myths related to the role of dirt, hygiene, and diet in causing acne. If a patient insists that particular fatty foods exacerbate acne, suggest that the patient undertake attempt to eat a healthier diet, as there is no known detriment to the avoidance of high-fat snacks.

Questions frequently arise regarding cosmetics and acne. In the past, researchers used animal models to test the comedogenic potential of raw materials used in cosmetics, and the term "acne cosmetica" was coined to describe acne suspected to be caused by cosmetic products. However, new evidence suggests that finished products formulated with "comedogenic" ingredients may not induce acne.²² Patients may, therefore, continue to use foundation, setting powder, blush, eye color, lip color, and any other cosmetics they wish. Despite the rarity of acne cosmetica, patients may feel more confident choosing cosmetics labeled as non-comedogenic/non-acnegenic.

Skin Care

Proper skin care is essential to support therapeutic outcomes and help minimize possible side effects of topical therapy. Moisturizers are known to provide benefits in the management of inflammatory skin diseases and have been recognized as important adjuncts to therapy.^{23,24} Specifically, studies show that concomitant use of effective moisturizers, mild cleansers and daily sunscreens enhance skin tolerance and comfort among individuals using topical retinoids.²⁵

Patients should not use soap to cleanse the face or, in the case of truncal acne, the chest and back. To wash the face each morning and evening, a mild, soap-free cleanser, such as Cetaphil (Galderma), Aquanil (PersonCovey), or CeraVe (Coria), should be applied with the fingertips and rinsed with water. A gentle moisturizer (such as CeraVe Moisturizer (Coria)) should be applied after cleansing.

Sun protection is essential. Patients should apply a broad-spectrum (UVA and UVB) sunscreen minimum SPF 15 to 30 to the face and all sun-exposed skin each morning. Rather than recommend a specific product, encourage patients to select the product of their choice; if they like the look, feel and smell of the formulation, they will want to use it.

Medications

Topical Therapy. A majority of patients with mild to moderate acne will be managed quite adequately with topical therapy alone. As noted above, 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.

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.²⁶⁻³⁰

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,^{1,31} data suggest topical retinoids may be underutilized.^{32,33}

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-dependant irritation has been noted, however, data show that 2.5% and 5% concentrations confer similar efficacy to 10% benzoyl peroxide.³⁴ Benzoyl peroxide is also shown to confer

comedolytic and keratolytic effects.³⁵

Topical antibiotics (clindamycin or erythromycin) also confer activity against *P. acnes* and have demonstrated anti-inflammatory effects.³⁶ Their use as monotherapy has largely diminished given the substantial body of data showing that use of BPO in combination with a topical antibiotic confers greater efficacy, enhances tolerability compared to either agent alone, and obviates concerns about developing resistance.³⁵

Several fixed-combination formulations are available that feature benzoyl peroxide along with clindamycin. A novel combination of benzoyl peroxide and adapalene is now available for once-daily use in the management of acne vulgaris. In trials, adapalene-BPO fixed-dose combination gel was more effective than either component as monotherapy, with safety similar to that of each component and vehicle.³⁷

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.³⁸

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.^{1,31,39} Given the

Acne Medication "Action" Chart				
Retinoids		Anticomedonal Effects	Anti-P. acnes	Anti-inflammatory
Tretinoin	<ul style="list-style-type: none"> • Generics • Retin-A Micro Pump 0.04%, 0.1% (Ortho Dermatologics) • Atralin 0.05% (Coria Laboratories) • Tretin-X 0.01%, 0.025%, 0.05%, 0.1% (Triax) 	+++	-	+
Adapalene	Differin Gel 0.1%, 0.3% (Galderma)	+++	-	+
Tazarotene	Tazorac Cream 0.1% (Allergan)	+++	-	+
Anti-microbial		Anticomedonal Effects	Anti-P. acnes	Anti-inflammatory
Benzoyl Peroxide	<ul style="list-style-type: none"> • NeoBenz Micro (Intendis) • Benzefoam 5.3% (Onset Therapeutics) • Benzagel 5%, 10% (Sanofi-Aventis) 		+++	+
Clindamycin or Erythromycin	<ul style="list-style-type: none"> • Cleocin T 1% (Pfizer) • Akne-mycin 2% (Coria) 		+++	+
Clindamycin/Benzoyl Peroxide	<ul style="list-style-type: none"> • Duac Gel, CLI 1%/BPO 5% (Stiefel) • BenzaClin, CLI 1%/BPO 5% (Sanofi-Aventis) • Acanya, CLI 1.2%/BPO 2.5%(Coria) 		+++	+
Other		Anticomedonal Effects	Anti-P. acnes	Anti-inflammatory
Dapsone	• Aczone gel 5% (Allergan)	-	-	+++
Adapalene/BPO	• Epiduo 0.1%/2.5% (Galderma)	++	+++	+
Clindamycin/Tretinoin	• Ziana, CLI 1.2%/tretinoin 0.025% (Medicis)	++	+++	+
+ signifies secondary effect		+++ signifies primary effect		- signifies no effect

Therapeutic Pearl: To minimize patient co-pay costs, many prescribers write for a three month supply. However, pharmacies increasingly will not dispense multi-month prescriptions. With a prescription for "Doryx 75mg, #90; One tablet PO, QD" a patient may receive just 30 pills with instructions to return for a refill. As noted, Doryx tablets can be broken in half without disrupting the delayed release mechanism, thereby preserving the beneficial GI effect profile. To save patients at least one month's copay, write for "Doryx 150mg #30" and instruct the patient to split the tablet in half, taking 75mg, which is one half tablet per, day.

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.

Systemic Therapy. Patients with moderate acne that does not adequately respond to topical therapy, who have a history of recurrence, or who have a significant inflammatory component to acne may be candidates for systemic therapy. Systemic antibiotics, which confer general anti-inflammatory effects and are able to reduce the number of

Propionibacterium acnes,⁴⁰ may also be useful for truncal acne when topical interventions present a treatment challenge due to difficulties in application.

Drugs of the tetracycline class, such as doxycycline and minocycline are considered first-line systemic antibiotic therapy for moderate to severe presentations.^{40,41} However, a review of case reports

Case 1

A 16-year-old female presents with grade I, mild acne of the face. The patient has mild post-inflammatory erythema (PIE).

The regimen for this patient should begin with regular use of sunscreens and mild skin-care: Aquanil, CeraVe Cleanser, or Cetaphil Gentle Skin Cleanser

Appropriate therapy for this type of presentation is once-daily, topical application of:

- **A retinoid:** Differin, Retin-A Micro, Tazorac, or generics

OR

- **A retinoid/BPO combination:** Epiduo

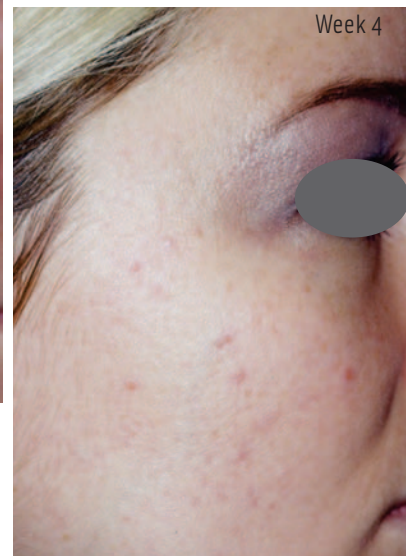
OR

- **A clindamycin/benzoyl peroxide combination:** Acanya, BenzaClin, Duac, or generic

A topical retinoid may be preferable to treat current lesions, prevent recurrence, and address PIE. Use of topical BPO in conjunction with topical clindamycin is important to help prevent bacterial resistance.



This patient was treated with a topical retinoid applied QHS.



Photos courtesy of Joseph Bikowski, MD and DermEdOnline.com

published between 1966 and 2003 found a lower rate of adverse events with doxycycline than with minocycline.⁴²

Minocycline has been shown to cause rare but potentially serious systemic adverse events, including autoimmune disorders such as lupus-like syndrome, hepatitis, and arthritis, as well as hypersensitivity reactions.⁴¹ A newer, extended-release minocycline formulation (Solydyn, Medicis) has been shown to significantly reduce inflammatory acne lesions while decreasing the rate of dose-dependent acute vestibular adverse events associated with minocycline.⁴³

Doxycycline may be associated with gastrointestinal side effects, especially with immediate release formulations. A slow-release formulation featuring enteric-coated doxycycline hyclate pellets encased in capsules (Doryx, Warner-Chilcott) is associated with significantly less nausea, vomiting, and abdominal discomfort compared to uncoated doxycycline hyclate powder encased in capsules.^{44,45} Of note, these tablets can be broken and even crushed and sprinkled over applesauce without impeding the slow-release mechanism.⁴⁶ Although doxycycline has been associated with photosensitivity, this phenomenon is uncommon, with no cases documented in the US from 1966 to 2003.⁴²

Case 2

A 14-year-old male presents with grade I, II, and III, moderate to severe acne of the face and neck.

He should be instructed to discontinue any OTC topical agents, use sun protection daily, and to cleanse affected areas with gentle cleansers: Aquanil, CeraVe Cleanser, or Cetaphil Gentle Skin Cleanser.

Appropriate therapy is

1. Topical:

- **A clindamycin/benzoyl peroxide combination:** Acanya, BenzaClin, Duac, or generic

AND

- **A retinoid:** Differin, Retin-A Micro, Tazorac, or generics

OR

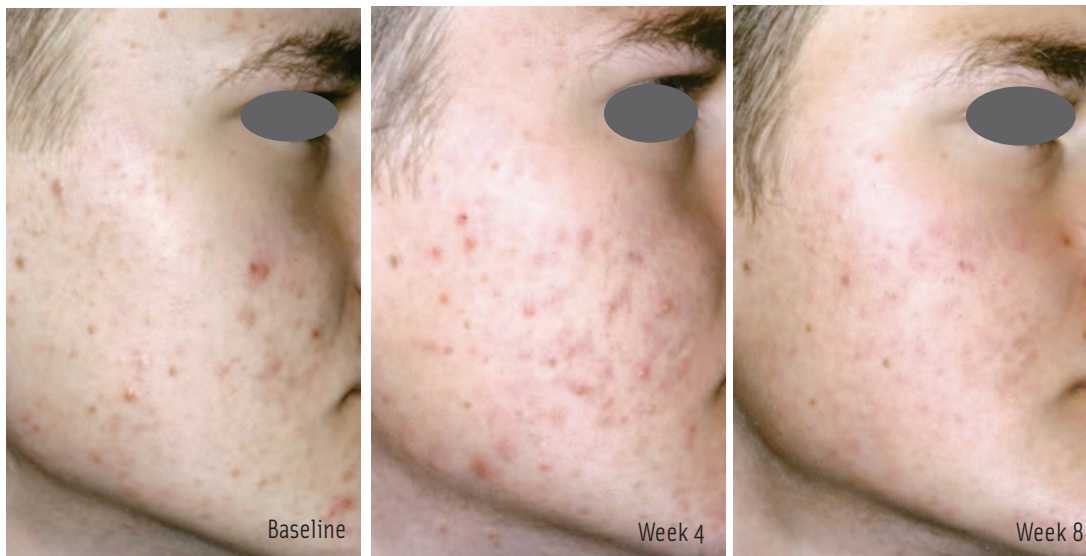
- **A retinoid/BPO combination:** Epiduo

This patient was treated with a topical retinoid QHS, topical clindamycin/BPO formulation QAM, and oral doxycycline QD.

2. Systemic

- **Antibiotic (minocycline or doxycycline):** Doryx, Dynacin, Minocin, Solodyn, or generic

The patient should be informed that the systemic antibiotic is intended for short-term control of acne and the topical regimen will be continued for long-term maintenance. Use of topical benzoyl peroxide in conjunction with the oral antibiotic is important to minimize reliance on the systemic agent and help prevent bacterial resistance. If improvement is not seen at week 4, consider referral to a dermatologist.



Photos courtesy of Joseph Bikowski, MD and DermEdOnline.com

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.⁴⁷ In addition, a topical retinoid is of primary value in acne management and may be used in conjunction with a systemic antibiotic. ■

Dr. Bikowski has served on the speaker's bureau or advisory board or is a shareholder or consultant to Allergan, Coria, Galderma, Stiefel/GlaxoSmithKline, Intendis, Medicis, Promius, Quinova, Ranbaxy, and Warner-Chilcott.

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