

A Consensus on Acne Management Focused on Specific Patient Features

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Background: Most treatment guidelines for acne are based on clinical severity. Our objective was to expand that approach to one that also comprised individualized patient features: a case-based approach.

Methods: An expert panel of Canadian dermatologists was established to develop demographic and clinical features considered to be particularly important in acne treatment selection. A nominal group consensus process was used for inclusion of features and corresponding appropriate treatments.

Results: Consensus was achieved on the following statements: follicular epithelial dysfunction contributes to acne pathogenesis; inflammation from underlying disease(s) or prior treatment may impact further patient management; management focusing on specific patient features and on addressing psychosocial factors, including impact on quality of life, may improve treatment adherence and outcomes; and case-based scenarios are a practical approach to illustrate the effect of these factors. To address the latter, eight case profiles were developed.

Conclusions: Management of acne should be based on multifactorial considerations beyond clinically determined acne severity and should include patient-reported impact, gender, skin sensitivity (including preexisting dermatoses), and phototype.

Contexte: La plupart des lignes directrices sur le traitement de l'acné reposent sur la gravité clinique de l'affection. L'étude avait pour but d'élargir l'approche et de l'adapter aux caractéristiques individuelles, ce qui en fait une approche basée sur les cas.

Méthode: Un groupe d'experts composé de dermatologues canadiens a été formé pour dresser la liste des caractéristiques démographiques et cliniques particulièrement importantes à tenir compte dans le choix du traitement de l'acné. La sélection des caractéristiques et des traitements appropriés correspondants a suivi un processus consensuel établi selon la technique du groupe nominal.

Résultats: Il y a eu consensus sur les énoncés suivants: un dysfonctionnement épithélial folliculaire joue un rôle dans la pathogenèse de l'acné; l'inflammation liée à des états pathologiques sous-jacents ou à des traitements antérieurs peut influencer sur la prise en charge ultérieure; une prise en charge adaptée aux caractéristiques individuelles et tenant compte des facteurs psychosociaux, dont la qualité de vie, peut améliorer le respect du traitement et les résultats cliniques; des scénarios basés sur des cas sont un moyen pratique d'illustrer l'effet de ces facteurs. Huit tableaux ont ainsi été élaborés afin d'expliquer ce dernier élément.

Conclusions: Outre le degré de gravité clinique, la prise en charge de l'acné devrait tenir compte de plusieurs facteurs, dont les effets déclarés par les patients, le sexe, la sensibilité de la peau (y compris les dermatoses préexistantes), et le phototype.

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A *CNE VULGARIS* is a chronic inflammatory dermatosis consisting of characteristic lesions composed of open and closed comedones, papules, pustules, and nodules.^{1,2} Cysts, dyspigmentation, and scarring can also be present as secondary features of acne. It is common, affecting 85 to 90% of teenagers and individuals of all ethnicities.^{3–6} In Canada, the prevalence of acne is estimated at about 2 million.⁷

Acne vulgaris is related to hormonal factors producing excess sebum, leading to proliferation of *Propionibacterium acnes*, inflammation, and infundibular hyperkeratiniza-

tion.^{2–4,6–9} More recent pathogenic advances include immunologic changes, inflammatory responses, altered sebum lipid quality, dysregulation of local sebaceous gland steroidogenesis, interaction with neuropeptidases, androgen activity, and nutrition.^{8–11}

A variety of evidence-based acne treatment guidelines are available to support the clinician in the selection of acne treatment.^{1,4} However, depending on factors such as local health care systems, the availability of products, and other locoregional issues, recommended treatment options will vary. Most treatment guidelines for acne are based on clinical severity and corresponding treatment selection. However, we posit that accounting for individual clinical features when making recommendations in various settings, such as by general practitioners and dermatologists, may optimize treatment and potentially improve outcomes. Our objective was to expand the acne treatment strategy beyond the conventional severity-based approach to one incorporating demographic and clinical features.

Methods

Literature Search

A literature review was conducted using the *Medline*, *Embase*, and *Cochrane* databases. The first search focused on recent developments in acne pathogenesis, acne treatment selection relevant to Canada, and acne patient case profiles. The search dates were July 8, 2012, to July 10, 2012.

A second literature search was conducted for reports relevant to defining specific acne patient features and case scenarios. This was conducted with the delimiting dates July 15, 2012, to July 16, 2012, and used the following keywords: *acne pathogenesis; acne patient profile; acne and skin barrier dysfunction; acne and psychosocial factors; acne and quality of life; tools for choosing topical and systemic acne treatment; adjunctive acne treatment; adherence; concordance; efficacy; safety; tolerability; dry skin; skin irritation; acne scarring; and treatment of acne scarring*. Exclusion criteria were no original data (unless a review article was deemed relevant), not dealing with the management of acne, and publication language other than English, German, or French.

The literature search findings were evaluated with the modified Scottish Intercollegiate Guidelines Network (SIGN). These grades of recommendation relate to the strength of the evidence and have previously been used in the development of guidelines in health care:

A: Randomized, double-blind clinical trial of high quality (e.g., sample size calculation, flow chart of patient inclusion, intention-to-treat analysis, sufficient sample size)

B: Randomized clinical trial of lesser quality (e.g., only single-blind, limited sample size: at least 15 patients per study arm)

C: Comparative trial with severe methodological limitations (e.g., not blinded, very small sample size, no randomization)

Development of Propositions for Specific Patient Features and Case Scenarios

A working committee of two dermatologists (C.L. and J.T.) and a scientific advisor (A.A.) identified individual patient features relevant to acne treatment selection. Case scenarios were developed to highlight these features.

Expert Panel

An expert panel of 13 Canadian dermatologists was convened for a 1-day meeting (September 15, 2012; Toronto, ON) to evaluate and deliberate patient-specific features that may influence acne therapy selection. Furthermore, this group was asked to propose treatment options appropriate to these identified features. The panel voted on propositions for patient features relevant to acne treatment selection considered important for inclusion and case development. Cases previously developed by the working committee were presented, and the panel voted on their inclusion after nominal group discussion. Consensus required a minimum of 90% agreement.

Statements Defined by the Panel

Clinical practice guidelines assist doctors in selection of acne treatments.^{1,12–14} However, the primary focus on treatment selection is clinical severity—a factor that does not adequately account for patient-specific features. For individual patients, the nuanced selection of treatment is more complex.

Based on the literature findings, the following statements were proposed and submitted to the panel for discussion, feedback, and voting:

1. Inflammation from underlying disease(s) or prior treatment may impact further patient management
2. Ongoing management with a focus on individual patient considerations may improve adherence and outcomes

3. A patient-centered approach addressing acne impact can improve treatment adherence and outcomes
4. Case-based scenarios are a practical approach to illustrate patient care strategies

1. *Follicular epithelial dysfunction contributes to acne pathogenesis (Table 1)*

Acne is a disease primarily of adolescence triggered by initiation of androgen production by the adrenal glands and gonads and usually subsides after this developmental phase.^{11,15} However, acne may persist beyond adolescence or occur for the first time in a significant proportion of individuals, particularly women.^{1,16} Hereditary mechanisms may be causal in some, including the abnormal gene expression for cytochrome P-450-1A1 and steroid-21-hydroxylase.^{1,15} Racial and ethnic factors are suggested to contribute to differences in the prevalence, severity, clinical presentation, and sequelae of acne.¹⁵ The pathogenesis of acne is frequently described as involving the following primary factors: excess sebum production, *P. acnes* proliferation, infundibular hyperkeratinization, inflammation, and androgens.²⁻⁵

2. *Inflammation from underlying disease(s) or resulting from prior treatment may impact further patient management (Table 2)*

More recently, it has become clear that underlying barrier dysfunction plays a role in the pathogenic pathway to acne^{6,8,9} (Figure 1). The sebaceous gland, as a neuroendocrine organ, locally responds to stress and infection.¹⁷⁻²¹ Sebum production by the sebaceous gland, *P. acnes* follicular colonization, alteration in the keratinization process, and release of inflammatory mediators into the skin have been described as primary pathogenic factors.¹⁸⁻²² These interact in a complex manner and play crucial roles in acne development.^{21,22} In view of the ubiquity of *P. acnes* in the general population, its role in acne is considered proinflammatory in predisposed individuals rather than infectious.^{21,22} Ongoing inflammation in acne is dependent on cell-mediated immune responses.²⁰⁻²² Therefore, the focus of

acne treatment is to target the multiple pathogenic factors and achieve improvement or clearance of acne while minimizing sequelae such as psychosocial impact, dyspigmentation, and scarring.²²

3. *Ongoing management with a focus on individual patient considerations can improve adherence and outcomes (Table 3)*

Beyond clinical acne severity grading, acne scarring, and postinflammatory pigmentary changes, patient assessment should also comprise an appropriately directed medical and dermatologic inquiry. In particular, a history of inflammatory dermatosis; age; gender; skin sensitivity; psychosocial factors including impact of acne; recurrence frequency; previous and current treatment; adjunctive skin care including skin care regimen; and a history of treatment adherence should be sought.¹³ Identifying patient-specific issues, such as adverse reactions to treatments and dry and/or sensitive skin, may rationalize future treatment selection.²³⁻²⁶

Treatment advice should include cleansing, moisturization, and cosmetic skin care regimens as well as nutrition (Figure 2).^{13,14} As multiple factors are involved in the pathogenesis of acne, combining treatments to target different pathophysiologic factors was suggested as a practical and effective option.²⁷⁻³³

Although poor adherence to acne therapy is multifactorial, a frequent reason for poor adherence to topical treatment is skin dryness and irritation.^{29,31} This may be attenuated with the use of gentle cleansers and noncomedogenic moisturizers to minimize barrier disruption and assist in barrier repair.^{32,34}

4. *An approach addressing psychosocial factors, including acne impact, can improve treatment adherence and outcomes (Table 4)*

Studies on psychosocial factors impacting acne treatment adherence and outcome are sparse.²⁴ An observational study evaluating demographic factors and clinical and patient-reported severity measures with adherence to topical acne treatments showed that adherence increases with impact on quality of life but decreases with increasing acne severity.²⁴

Table 1. Follicular Epithelial Dysfunction Contributes to Acne Pathogenesis

Authors/Year	Results
Bhambri et al/2009 ²	Acne is an inflammatory disorder of pilosebaceous units, with characteristic lesions
Gollnick/2003 ⁴	Focus of treatment is to be targeted on the reduction in inflammatory mediators
Kurokawa et al/2009 ⁶	Skin barrier dysfunction coupled with various triggering events contributes to the signs and symptoms of acne
Jeremy et al/2003 ⁸	In acne-affected skin, phytosphingosine is depleted, making the skin prone to inflammation
Trivedi et al/2006 ²²	Underlying barrier dysfunction plays a crucial role in triggering the pathogenic pathway leading to acne



Table 2. Inflammation from Underlying Disease(s) or Prior Treatment May Impact Further Patient Management

Authors/Year	Results
Gollnick et al/2003 ¹²	Inflammation may be primary rather than secondary
Ingram et al/2010 ¹³	Reduction of inflammation is a key aspect of acne treatment
Strauss et al/2007 ¹⁴	Skin barrier dysfunction contributes to the development of acne
Jeremy et al/2003 ⁸	Acne-affected skin is prone to inflammation
Kapetanovic and Cavaillon/2007 ¹⁸	Inflammation is part of the pathogenic pathway leading to acne

The results from another study, however, suggested that a positive effect on adherence to acne treatment can be shown in subjects with more severe acne, particularly those on oral isotretinoin treatment.²⁸ Adherence is also improved in those using adjunctive treatment with moisturizers and cleansers.²⁹ Further studies indicated that clinical improvement evaluated by the dermatologist, patient satisfaction with therapy, and knowledge of acne treatment support patient adherence.^{4,27,28,30–32,35–37}

5. Case-based acne scenarios are a practical approach to optimize patient care

Patients affected by acne have many different features and expectations about treatment outcomes.^{23,24,32} Identification of specific individual concerns and issues before treatment selection may help increase patient adherence and improve outcomes.^{7–9,20} This, combined with treatment targeting the multiple acne pathways, is a rational approach to patient-focused treatment selection.^{18–22}

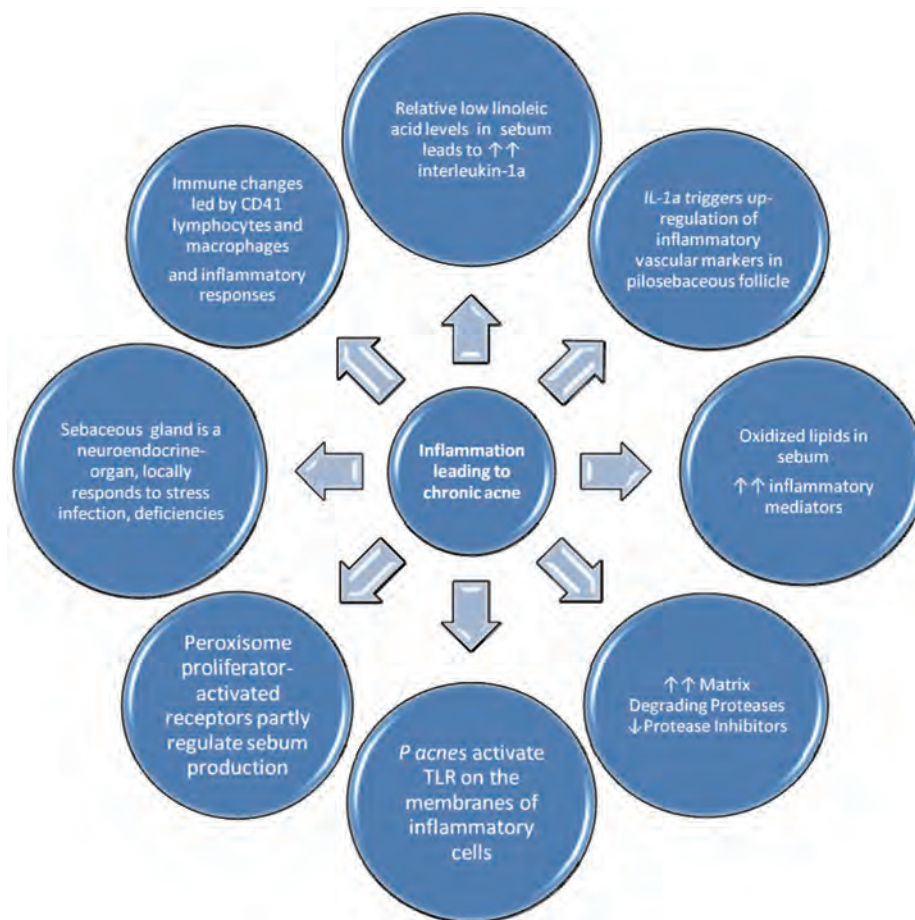


Figure 1. Pathogenesis of acne: recent insights. Adapted from Jugeau S et al and Kang S et al.^{19,20} IL-1a = interleukin-1a; TLR = Toll-like receptor.

Table 3. Ongoing Management with a Focus on Individual Patient Considerations Can Improve Adherence and Outcomes

Authors/Year	Results
Tan et al/2009 ²⁴	Adherence was significantly positively correlated with improved quality of life
Gollnick et al/2003 ¹²	Simplify treatment and make it more comfortable, causing less irritation and dryness
Yentzer et al/2010 ²⁸	Improving treatment, making it more comfortable with less skin irritation
Koo/2003 ³⁷	Complicated treatment regimen for children and the chronic nature of the disease and skin irritation lead to poor medication adherence
Yentzer et al/2010 ²⁷	More simple and combined regimens provide better outcomes
Bucks et al/2009 ³⁰	Combination treatment leads to better patient adherence

Specific Patient Features Translating to Individualized Acne Treatment Strategy

Although there are a plethora of acne grading scales available in the literature,¹ the panel opted for a practical classification tool that may be applied for this treatment strategy.⁷ A modification of the acne severity classification from the Euro S3 treatment guidelines for acne was used⁷: mild acne: comedonal, papular/pustular; moderate acne: severe papular/pustular and mild nodular; severe acne: nodular/conglobata.

Based on panel discussions, consensus was reached on the following patient-case profiles. Patients within each profile can present with varying levels of acne severity.

Patient education is a major factor that impacts adherence.³⁹ It is further important that health care providers educate patients about the expected outcomes of treatment, how long it typically takes to achieve improvement, and how acne management requires long-term therapy.^{24,39}

Case 1

Case 1 is a teenager (male or female) with oily, tolerant skin (mild: comedonal, papular/pustular; moderate: papular/pustular, nodular; severe: nodular/conglobata). Issues include the following: poor adherence to treatment; lack of understanding or acceptance that acne is a chronic disease that requires a disciplined approach long term and maintenance; and complicated treatment regimens, together with the chronic nature of the disease and skin irritation, lead to poor medication adherence. The approach should proceed as follows: provide education on the cause of acne and treatment options; offer a simplified treatment regimen to increase convenience; discuss realistic expectations of treatment; and discuss monitoring, follow-up, and the importance of adherence.

Treatment details are shown in Table 5.

Case 2

Case 2 is a female teenager with normal tolerant skin (mild: comedonal, papular/pustular; moderate: mixed and papular/pustular, nodular; severe: nodular/conglobata). Issues include the following: limited or no results with first-line over-the-counter therapy (e.g., 5% benzoyl peroxide [BPO], BPO wash, salicylic acid). If the psychosocial impact of acne is significant, the physician

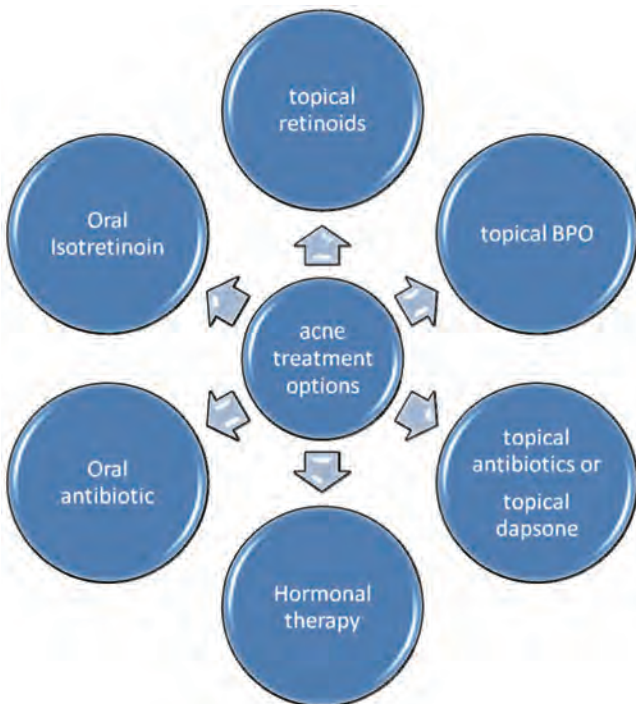


Figure 2. Medical treatment options for acne patients. These options can be combined in various permutations to enhance efficacy, convenience, and tolerability. Adapted from Nast A et al and Dréno B et al.^{1,40}



Table 4. A Patient-Centered Approach Addressing Psychosocial Factors Including Acne Impact Can Improve Treatment Adherence and Outcomes

<i>Authors/Year</i>	<i>Results</i>
Tan et al/2009 ²⁴	Patients rated side effects from the medication is reported as the most common reason for low adherence, followed by forgetfulness and lack of disease improvement
Dréno et al/2010 ³¹	Factors that had a positive effect on adherence were more severe acne; use of moisturizers, cleansers, either topical therapy alone or isotretinoin; good clinical improvement as evaluated by the dermatologist; patient satisfaction with therapy; and knowledge of acne treatment
Nast et al/2012 ¹	Treatment adherence is improved when regimes are simplified and comfortable

may use a more aggressive therapy. The approach should proceed as follows: education on the cause of acne and on the treatment provided; offering hormonal therapy (may be combined with a topical retinoid and a topical antimicrobial or antibiotic); discussing realistic expectations of treatment; and discussing monitoring and follow-up of treatment.

Treatment details are shown in Table 6.

Case 3

Case 3 is a teenager (male or female) with sensitive skin and/or a history of atopic dermatitis (mild: comedonal, mixed and papular/pustular; moderate: mixed and papular/pustular, nodular; severe: nodular/conglobata). Issues include the following: skin barrier disorder; prone to

cutaneous subacute and chronic inflammation; dryness, peeling, and irritation resulting from acne therapy; and poor adherence as a result of cutaneous intolerance to acne therapy. The approach should proceed as follows: education on the cause of acne and education on treatment options; offering a simplified, well-tolerated treatment regimen; discussing patient expectations of treatment outcome; discussing monitoring and follow-up of treatment; and recommending adjunctive treatment with gentle cleansers and moisturizers.

Treatment details are shown in Table 7.

Case 4




Case 4 is a patient (adult male or female) with sensitive skin or a history of atopic dermatitis (mild: comedonal,

Table 5. Case 1: Teenager (Male or Female) with Oily, Tolerant Skin

<i>Treatment</i>	<i>Noninflammatory Lesions</i>		<i>Inflammatory Lesions</i>	
	<i>Mild Comedonal, Papular/Pustular</i>	<i>Moderate Papular/Pustular, Nodular</i>	<i>Severe Nodular/Conglobata</i>	
First line	Topical retinoid or BPO	BPO/antibiotic or Retinoid/antibiotic or Topical retinoid/BPO	Same as first line mild: inflammatory plus consider adding oral antibiotic or BCP (female)	Oral isotretinoin
Second line	Topical retinoid/BPO	Topical dapsone	Oral antibiotic or BCP (female)	BCP (female)

BCP = birth control pill; BPO = benzoyl peroxide.

Table 6. Case 2: Female Teenager with Normal Tolerant Skin

			
	<i>Mild Comedonal, Papular/Pustular</i>	<i>Moderate Papular/Pustular, Nodular</i>	<i>Severe Nodular/Conglobata</i>
<i>Treatment</i>	<i>Noninflammatory Lesions</i>	<i>Inflammatory Lesions</i>	
First line	Topical retinoid ± BPO	Topical BPO/antibiotic or Topical retinoid/BPO or Topical retinoid/AB	Topical retinoid/antibiotic or Topical BPO/antibiotic or BCP ± oral antibiotic
Second line	Topical retinoid/antibiotic	Topical dapsone	Topical dapsone or Oral antibiotic ± BCP

BCP = birth control pill; BPO = benzoyl peroxide.

mixed and papular/pustular; moderate: mixed and papular/pustular; severe: nodular/conglobata). Issues include the following: skin barrier disorder; prone to cutaneous subacute and chronic inflammation; and dryness, peeling, and irritation also resulting from acne therapy. The approach should proceed as follows: education on the cause of acne and on treatment options; discussing realistic expectations of treatment; discussing monitoring and follow-up of treatment; and




recommending adjunctive treatment with cleansers and moisturizers.

Treatment details are shown in Table 8.

Case 5

Case 5 is an adult female patient with a very stressful job; acne seems to be related to the menstrual cycle (mild: comedonal, mixed and papular/pustular; moderate: mixed and papular/

Table 7. Case 3: Teenager (Male or Female) with Sensitive Skin and/or a History of Atopic Dermatitis

			
	<i>Mild Comedonal, Papular/Pustular</i>	<i>Moderate Papular/Pustular, Nodular</i>	<i>Severe Nodular/Conglobata</i>
<i>Treatment</i>	<i>Noninflammatory Lesions</i>	<i>Inflammatory Lesions</i>	
First line	Topical retinoid ± Topical antibiotic	Same as first line mild ± Oral antibiotic or BCP (female) or Topical dapsone	Oral isotretinoin or BCP (female)
Second line	Topical BPO ± Topical antibiotic or topical dapsone	Oral antibiotic	Oral isotretinoin ± BCP (female)

BCP = Birth control pill; BPO = benzoyl peroxide.

- Gentle cleanser and noncomedogenic moisturizer morning and night.
- When starting, apply for 5 minutes initially and slowly increase as tolerated. When tolerability is ensured, apply the topical every night.
- If irritation or dryness develops with topical treatment, reduce the frequency and/or duration of the topical treatment application.



Table 8. Case 4: Adult Patient (Male or Female) with Sensitive Skin



Mild Comedonal, Papular/Pustular



Moderate Papular/Pustular, Nodular



Severe Nodular/Conglobata

Treatment	Noninflammatory Lesions	Inflammatory Lesions		
First line	Topical retinoid	Topical retinoid ± Topical antibiotic or Topical dapsone	Same as first line mild or Oral antibiotic or BCP (female) or Topical dapsone	Oral isotretinoin or BCP (female)
Second line	Topical BPO	Topical BPO ± Topical AB or Topical dapsone	BCP (female)	Oral isotretinoin ± BCP (female)

BCP = birth control pill; BPO = benzoyl peroxide.

- Gentle cleanser and noncomedogenic moisturizer morning and night.
- When starting, apply for 5 minutes initially and slowly increase as tolerated. When tolerability is ensured, apply the topical every night.
- If irritation or dryness develops with topical treatment, reduce the frequency and/or duration of the topical treatment application.

pustular, nodular; severe: nodular/conglobata). Issues include the following: acne is mainly inflammatory in nature and often presents along the jawline and chin and in a perioral location and dryness, peeling, and irritation also resulting from acne therapy. The approach should proceed as follows: education on the cause of acne and on treatment options; discussing realistic expectations of treatment; discussing monitoring and follow-up of treatment; and recommending adjunctive treatment with cleansers and moisturizers.

Treatment details are shown in Table 9.

Case 6

Case 6 is an adult male or female patient with combined facial and truncal acne, mostly present on the upper back (mild: comedonal, mixed and papular/pustular; moderate: mixed and papular/pustular; nodular; severe: nodular/conglobata). Issues include the following: application on

Table 9. Case 5: Adult Female Patient with a Very Stressful Job; Acne Seems to Be Hormone Related



Mild Comedonal, Papular/Pustular



Moderate Papular/Pustular, Nodular






Severe Nodular/Conglobata

Treatment	Noninflammatory Lesions	Inflammatory Lesions		
First line	Topical retinoid or Topical retinoid/AB	Topical retinoid/antibiotic or Topical retinoid/BPO or BPO/antibiotic ± Topical dapsone	Same as first line mild or Oral antibiotics or BCP	Oral isotretinoin or BCP
Second line	Topical retinoid/BPO or Antibiotic/BPO	Topical dapsone	Oral antibiotic or BCP	Oral isotretinoin ± BCP

BCP = birth control pill; BPO = benzoyl peroxide.

Table 10. Case 6: Adult Patient (Male or Female) with Combined Facial and Truncal Acne

				
	<i>Mild Comedonal, Papular/Pustular</i>		<i>Moderate Papular/Pustular, Nodular</i>	<i>Severe Nodular/Conglobata</i>
<i>Treatment</i>	<i>Noninflammatory Lesions</i>	<i>Inflammatory Lesions</i>		
First line	Topical retinoid ± BPO wash	Topical retinoid/topical antibiotic	Same as first line mild or Oral antibiotics or BCP (female)	Oral isotretinoin ± BCP (female)
Second line	Topical retinoid/antibiotic	Topical dapsone	Oral antibiotic BCP (female)	Oral isotretinoin ± BCP (female)

BCP = birth control pill; BPO = benzoyl peroxide.

the back may be inconvenient using topical treatments and irritation caused by certain fabrics. The approach should proceed as follows: education on the cause of acne and on treatment options; discussing realistic expectations of treatment; discussing monitoring and follow-up of treatment; and recommending adjunctive treatment with cleansers and moisturizers.

Treatment details are shown in Table 10.




Case 7

Case 7 is a male or female patient postpuberty with skin of color and facial acne (mild: comedonal, mixed and papular/pustular; moderate: mixed and papular/pustular,

nodular; severe: nodular/conglobata). Issues include the following: dryness, peeling, and irritation also resulting from acne therapy; some topical treatments (eg, BPO) may leave visible “white film” on skin of color; and postinflammatory hyperpigmentation (PIH) and keloidal scarring being more prevalent in skin of color acne patients. The approach should proceed as follows: education on the cause of acne and on treatment options provided; discussing realistic expectations of treatment; discussing monitoring and follow-up of treatment; considering less irritating forms of topical retinoids and lower concentrations of BPO to minimize irritation and to minimize the risk of treatment-related PIH; and providing adjunctive treatment with cleansers and moisturizers.

Treatment details are shown in Table 11.

Table 11. Case 7: Adult Patient (Male or Female) Skin of Color

				
	<i>Mild Comedonal, Papular/Pustular</i>		<i>Moderate Papular/Pustular, Nodular</i>	<i>Severe Nodular/Conglobata</i>
<i>Treatment</i>	<i>Noninflammatory Lesions</i>	<i>Inflammatory Lesions</i>		
First line	Topical retinoid	Topical dapsone	Same as first line mild + Oral antibiotic or BCP (female)	Oral isotretinoin ± BCP (female)
Second line	Topical retinoid/antibiotic or Topical dapsone		Topical dapsone ± BCP (female)	Oral isotretinoin ± BCP (female)

BCP = birth control pill; BPO = benzoyl peroxide.



Table 12. Case 8: Pregnant Patient with Facial Acne Who Plans to Nurse for about 6 Months

Treatment	Mild Comedonal, Papular/Pustular			
	Noninflammatory Lesions	Inflammatory Lesions	Moderate Papular/Pustular, Nodular	Severe Nodular/Conglobata
First line	BPO ± Topical antibiotic		Topical antibiotic/BPO	Refer to dermatologist
Second line	Refer to dermatologist			
Caution	Avoid retinoids (isotretinoin is contraindicated) and avoid tetracyclines			

BCP = birth control pill; BPO = benzoyl peroxide.

Case 8

Case 8 is a pregnant patient with facial acne planning to nurse for 6 months (mild: comedonal, mixed and papular/pustular; moderate: mixed and papular/pustular, nodular; severe: nodular/conglobata). Issues include the following: concern about the safety of treatments during pregnancy and nursing. The approach should proceed as follows: education on the cause of acne and on the treatment provided, specifically addressing why topical retinoids may be relatively contraindicated and certain oral antibiotics, hormonal treatments, and oral retinoids should be avoided; discussing realistic expectations of treatment; discussing monitoring and follow-up of treatment; and recommending adjunctive treatment with cleansers and moisturizers.

Treatment details are shown in Table 12.

Using multiple agents at the same time during treatment (concomitant therapy) has been recommended as a rational means to achieve an optimal outcome.¹² Acne therapy in skin of color (high melanin content) presents unique challenges due to differences relating to acne sequelae in these skin types, especially the presence or risk of PIH and keloidal scarring,³⁹ which are more prevalent in darker skin. It is proposed that acne-related PIH is caused by a response to skin inflammation.^{12,39} Therefore, minimizing inflammation and reducing potential irritation and dryness are key goals in treating acne, especially in skin of color.^{12,40,41}

Specific Patient Features and Acne Treatment

In view of recent developments in acne pathogenesis,^{8,17–22} case scenarios were developed to illustrate individualized treatment strategies. The population affected by acne is individually characterized by a multiplicity of differing features beyond objective severity, including age, gender, phototype, skin sensitivity, and quality of life impact.²⁴

Identification of specific factors that can influence outcomes may provide a means to provide more effective treatments with the least risk of intolerance. Such a strategy may lead to increased patient adherence, improved outcomes, and greater patient satisfaction with care.^{27,28}

Various clinical practice guidelines and other tools for selecting acne treatment are available.^{1,30} For the case-

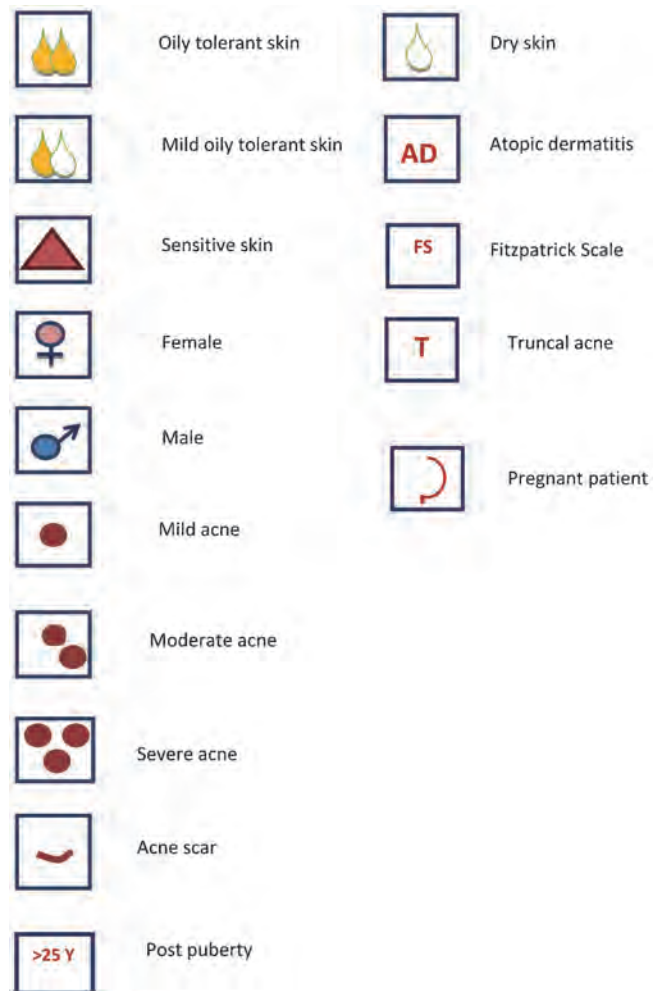


Figure 3. Symbols to identify patient characteristics.

based scenarios, the evidence provided from the European Evidence-based (S3) Guidelines for the Treatment of Acne¹ was used as guidance for treatment proposals, together with the information obtained from the Global Alliance to Improve Outcomes in Acne.³¹ The panel members discussed, voted in a nominal group process, and reached consensus (90% of the vote) on specific approaches to acne management within the scope of

treatments available in Canada. The SIGN system for levels of evidence was used to grade the recommendations for acne treatment:

1. Depending on the degree of inflammation, a topical retinoid may be used either alone or with BPO (when comedones predominate) or in combination with other topical agents and oral medications^{13,27,30} (Grade A).

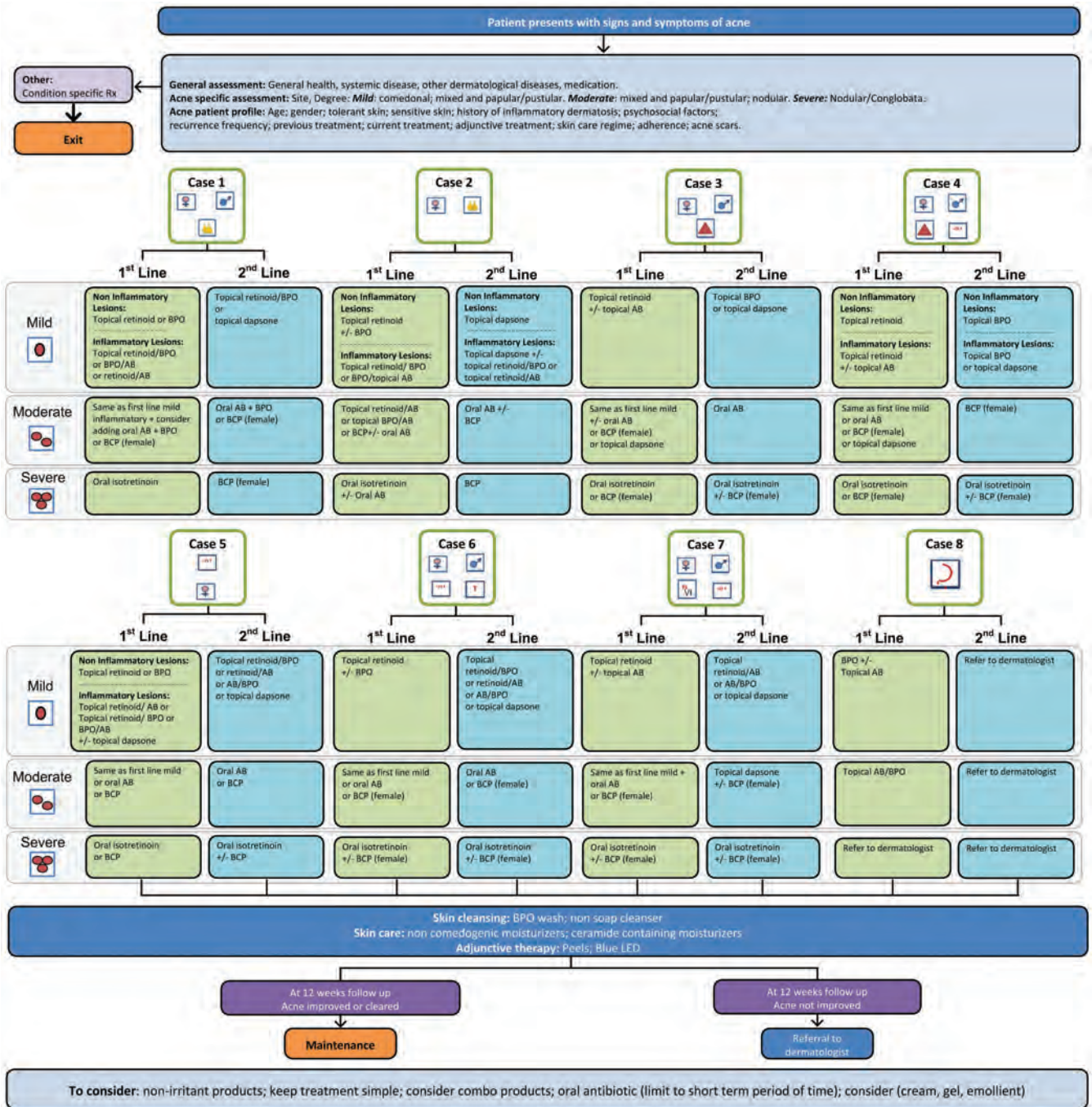


Figure 4. Acne management strategy focused on specific patient features. AB = antibiotic; BCP = birth control pill; BPO = benzoyl peroxide.



2. Female patients also may benefit from hormonal therapy with oral contraceptives, which may be combined with topical medications^{13,14,27,35,36} (Grade A).

The beneficial effects of combining acne agents include targeting different pathophysiologic factors (i.e., abnormal desquamation, *P. acnes* proliferation, and inflammation), increasing efficacy, improving the rapidity of lesion resolution, and minimizing the potential for antibiotic resistance^{1,35} (Grade B). Fixed-dose combination products have the further benefit of increased convenience and may improve adherence. Combination therapy, comprising permutations of topical retinoid, BPO, antibiotics (topical or oral), and hormonal therapy, is now considered the standard of care for the majority of patients with acne^{1,31,41} (Grade A). Monotherapy with a topical antibiotic is discouraged and other alternatives are proposed, such as combinations with BPO to prevent sensitizing and resistance.^{1,23,31,41}

3. For severe acne, treatment with oral isotretinoin is recommended^{1,13,14,27} (Grade A). Isotretinoin therapy also should be considered if oral contraceptive use in women was unsuccessful or for cases of acne that are refractory to conventional therapy with a topical retinoid, BPO, and oral antibiotic therapy (see Figure 2)^{1,31} (Grade B).
4. After acne therapy was successful, maintenance treatment is to be commenced to prevent recurrence. Topical retinoid, adapalene, and tazorac may be considered for acne patients' maintenance therapy as well as combination therapy of adapalene-BPO gel (Grade A). Hydration of the skin using an effective moisturizer is one of the important measures involved in preserving the integrity of the stratum corneum barrier and may reduce skin irritation during acne treatment (Grade C).

Symbols were developed to easily identify patient characteristics (Figure 3) that may underlie specific treatment recommendations. Details on this treatment strategy are shown in Figure 4.

Conclusion

The case-centered approach presented herein more realistically mimics patient presentations as it is based on multifactorial considerations beyond objective acne severity, including patient-reported impact, gender, skin sensitivity, concomitant skin conditions, and phototype. This treatment strategy may facilitate selection of individualized options based on consideration of the multifaceted features rather than the more unidimensional approach of conventional treatment guidelines.

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References

- Nast A, Dreno B, Bettoli V, et al. European evidence-based (S3) guidelines for the treatment of acne. *J Eur Acad Dermatol Venereol* 2012;26 Suppl 1:1–29.
- Bhambri S, Del Rosso JQ, Bhambri A. Pathogenesis of acne vulgaris: recent advances. *J Drugs Dermatol* 2009;8:615–8.
- James WD. Acne. *N Engl J Med* 2005;352:1463–72, doi:[10.1056/NEJMcp033487](https://doi.org/10.1056/NEJMcp033487).
- Gollnick H. Current concepts of the pathogenesis of acne: implications for drug treatment. *Drugs* 2003;63:1579–96, doi:[10.2165/00003495-200363150-00005](https://doi.org/10.2165/00003495-200363150-00005).
- Perkins A, Cheng C, Hillebrand G, et al. Comparison of the epidemiology of acne vulgaris among Caucasian, Asian, Continental Indian and African American women. *J Eur Acad Dermatol Venereol* 2010;25:1054–60, doi:[10.1111/j.1468-3083.2010.03919.x](https://doi.org/10.1111/j.1468-3083.2010.03919.x).
- Kurokawa I, Danby FW, Ju Q, et al. New developments in our understanding of acne pathogenesis and treatment. *Exp Dermatol* 2009;18:821–32, doi:[10.1111/j.1600-0625.2009.00890.x](https://doi.org/10.1111/j.1600-0625.2009.00890.x).
- Tan JK, Tang J, Fung K, et al. Development and validation of a comprehensive acne severity scale. *J Cutan Med Surg* 2007;11:211–6.
- Jeremy AH, Holland DB, Roberts SG, et al. Inflammatory events are involved in acne lesion initiation. *J Invest Dermatol* 2003;121:20–7, doi:[10.1046/j.1523-1747.2003.12321.x](https://doi.org/10.1046/j.1523-1747.2003.12321.x).
- Goulden V, Stables GI, Cunliffe WJ. Prevalence of facial acne in adults. *J Am Acad Dermatol* 1999;41:577–80.
- Dréno B, Poli F. Epidemiology of acne. *Dermatology* 2003;206:7–10, doi:[10.1159/000067817](https://doi.org/10.1159/000067817).
- Cordain L, Lindeberg S, Hurtado M, et al. Acne vulgaris: a disease of Western civilization. *Arch Dermatol* 2002;138:1584–90, doi:[10.1001/archderm.138.12.1584](https://doi.org/10.1001/archderm.138.12.1584).
- Gollnick H, Cunliffe W, Berson D, et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol* 2003;49(1 Suppl):S1–37, doi:[10.1067/mjd.2003.618](https://doi.org/10.1067/mjd.2003.618).



13. Ingram JR, Grindlay DJ, Williams HC. Management of acne vulgaris: an evidence-based update. *Clin Exp Dermatol* 2010;35:351–4, doi:[10.1111/j.1365-2230.2009.03683.x](https://doi.org/10.1111/j.1365-2230.2009.03683.x).
14. Strauss JS, Krowchuk DP, Leyden JJ, et al. Guidelines of care for acne vulgaris management. *J Am Acad Dermatol* 2007;56:651–63, doi:[10.1016/j.jaad.2006.08.048](https://doi.org/10.1016/j.jaad.2006.08.048).
15. Herane MI, Ando I. Acne in infancy and acne genetics. *Dermatology* 2003;206:24–8, doi:[10.1159/000067819](https://doi.org/10.1159/000067819).
16. Vowels BR, Yang S, Leyden JJ. Induction of proinflammatory cytokines by a soluble factor of *Propionibacterium acnes*: implications for chronic inflammatory acne. *Infect Immun* 1995;63:3158–65.
17. Holland DB, Jeremy AH. The role of inflammation in the pathogenesis of acne and acne scarring. *Semin Cutan Med Surg* 2005;24:79–83, doi:[10.1016/j.sder.2005.03.004](https://doi.org/10.1016/j.sder.2005.03.004).
18. Kapetanovic R, Cavaillon JM. Early events in innate immunity in the recognition of microbial pathogens. *Expert Opin Biol Ther* 2007;7:907–18, doi:[10.1517/14712598.7.6.907](https://doi.org/10.1517/14712598.7.6.907).
19. Jugeau S, Tenaud I, Knol AC, et al. Induction of toll-like receptors by *Propionibacterium acnes*. *Br J Dermatol* 2005;153:1105–13, doi:[10.1111/j.1365-2133.2005.06933.x](https://doi.org/10.1111/j.1365-2133.2005.06933.x).
20. Kang S, Cho S, Chung JH, et al. Inflammation and extracellular matrix degradation mediated by activated transcription factors nuclear factor-kappaB and activator protein-1 in inflammatory acne lesions in vivo. *Am J Pathol* 2005;166:1691–9, doi:[10.1016/S0002-9440\(10\)62479-0](https://doi.org/10.1016/S0002-9440(10)62479-0).
21. Kim J, Ochoa MT, Krutzik SR, et al. Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses. *J Immunol* 2002;169:1535–41.
22. Trivedi NR, Cong Z, Nelson AM, et al. Peroxisome proliferator-activated receptors increase human sebum production. *J Invest Dermatol* 2006;126:2002–9.
23. Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. *J Am Acad Dermatol* 2003;49(3 Suppl):S200–10, doi:[10.1067/S0190-9622\(03\)01154-X](https://doi.org/10.1067/S0190-9622(03)01154-X).
24. Tan JK, Balagurusamy M, Fung K, et al. Effect of quality of life impact and clinical severity on adherence to topical acne treatment. *J Cutan Med Surg* 2009;13:204–8.
25. Lee IA, Maibach HI. Pharmionics in dermatology: a review of topical medication adherence. *Am J Clin Dermatol* 2006;7:231–6, doi:[10.2165/00128071-200607040-00004](https://doi.org/10.2165/00128071-200607040-00004).
26. Bucks DAW, Pillai RS, McCall-Perez F. Advances in formulation technologies: creating highly effective and well-tolerated topical dermatologicals. *Skin Aging* 2010;Suppl:4–6.
27. Yentzer BA, Ade RA, Fountain JM, et al. Simplifying regimens promotes greater adherence and outcomes with topical acne medications: a randomized controlled trial. *Cutis* 2010;86:103–8.
28. Yentzer BA, Baldwin H, Shalita A, et al. Optimizing patient adherence: update on combination acne therapy – teens and beyond. *J Drugs Dermatol* 2010;9:s92–5.
29. Feldman SR, Chen DM. How patients experience and manage dryness and irritation from acne treatment. *J Drugs Dermatol* 2011;10:605–8.
30. Bucks D, Sarpotdar P, Yu K, et al. The development and optimization of a fixed combination of clindamycin and benzoyl peroxide aqueous gel with minimal irritation and enhanced bioavailability. *J Drugs Dermatol* 2009;8:634–8.
31. Dréno B, Thiboutot D, Gollnick H, et al. Global Alliance to Improve Outcomes in Acne. Large-scale worldwide observational study of adherence with acne therapy. *Int J Dermatol* 2010;49:448–56, doi:[10.1111/j.1365-4632.2010.04416.x](https://doi.org/10.1111/j.1365-4632.2010.04416.x).
32. Draeos ZD, Callender V, Young C, Sunil SD. The effect of vehicle formulation on acne medication tolerability. *Cutis* 2008;82:281–4.
33. Elias PM, Hatnano Y, Williams ML. Skin barrier dysfunction mechanisms in inflammatory dermatosis. *J Allergy Clin Immunol* 2008;121:1337–43, doi:[10.1016/j.jaci.2008.01.022](https://doi.org/10.1016/j.jaci.2008.01.022).
34. Raimer S, Maloney JM, Bourcier M, et al. United States/Canada Dapsone Gel Study Group. Efficacy and safety of dapsone gel 5% for the treatment of acne vulgaris in adolescents. *Cutis* 2008;81:171–8.
35. Piette WW, Taylor S, Pariser D, et al. Hematologic safety of dapsone gel, 5%, for topical treatment of acne vulgaris. *Arch Dermatol* 2008;144:1564–70, doi:[10.1001/archdermatol.2008.518](https://doi.org/10.1001/archdermatol.2008.518).
36. Fitzpatrick TB. Soleil et peau. *J Med Esthet* 1975;2:330–4.
37. Koo J. How do you foster medication adherence for better acne vulgaris management? *Skinmed* 2003;2:229–33, doi:[10.1111/j.1540-9740.2003.02037.x](https://doi.org/10.1111/j.1540-9740.2003.02037.x).
38. Thiboutot DM, Weiss J, Bucko A, et al. Adapalene-benzoyl peroxide, a fixed-dose combination for the treatment of acne vulgaris: results of a multicenter, randomized double-blind, controlled study. *J Am Acad Dermatol* 2007;57:791–9, doi:[10.1016/j.jaad.2007.06.006](https://doi.org/10.1016/j.jaad.2007.06.006).
39. Cheng CE, Irwin B, Mauriello D, et al. Self-reported acne severity, treatment, and belief patterns across multiple racial and ethnic groups in adolescent students. *Pediatr Dermatol* 2010;27:446–52, doi:[10.1111/j.1525-1470.2010.01286.x](https://doi.org/10.1111/j.1525-1470.2010.01286.x).
40. Dréno B, Bettoli V, Ochsendorf F, et al. An expert view on the treatment of acne with systemic antibiotics and/or oral isotretinoin in the light of the new European recommendations. *Eur J Dermatol* 2006;16:565–71.
41. Segransky M, Yentzer BA, Feldman SR. Benzoyl peroxide: a review of its current use in the treatment of acne vulgaris. *Expert Opin Pharmacother* 2009;10:2555–62, doi:[10.1517/14656560903277228](https://doi.org/10.1517/14656560903277228).

