

# Research Review™

## EDUCATIONAL SERIES

### Skin Care in the Management of Acne Vulgaris

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This review is a summary of acne vulgaris and its management, with particular emphasis on the importance of skin care, comprising skin cleansing and moisturisation, in the treatment of acne.

#### Introduction

Acne vulgaris (common acne) is a chronic skin condition characterised by inflammation of the pilosebaceous units (hair follicles and their sebaceous gland). It predominantly affects adolescents and young adults,<sup>1,2</sup> although the pre-pubertal and adult subgroups are increasingly being seen. Acne can present as non-inflammatory lesions, inflammatory lesions, or a mixture of both. Distribution is in most cases facial but can involve the neck, chest, and back.

#### Epidemiology

Acne is a common condition with its prevalence approaching 90% in school-age subjects.<sup>3</sup> There is large variation in prevalence rates among studies, which is likely due to the use of different methods to diagnose acne and grade its severity and to differences in sample populations.

Acne usually begins in adolescence and is more frequent in males than females during their teenage years.<sup>2</sup> In NZ, a 1995 study of senior high school students found acne to be present in 91% of male and 79% of female students who had their acne objectively assessed by investigators, with acne being rated as severe in more males (7%) than females (1%).<sup>4,5</sup> A larger 2004 study of younger high school students found a 67% overall prevalence of self-reported acne, with 'problem acne' reported by more female (23%) than male (16%) students.<sup>6</sup>

Acne usually resolves in early adulthood (by the age 25 years) but it can persist well into adulthood and even start in adulthood, especially in women.<sup>2</sup> A large community-based study of adults aged >25 years in the US showed some degree of acne present in 54% of women and 40% of men, with clinical acne being noted in 12% of women and 3% of men.<sup>7</sup> Eighteen percent of women and 8% of men over the age of 25 years were reported to have late-onset acne in one UK study.<sup>8</sup>

Although acne typically begins in adolescence, early-onset acne can occur in many children due to the early onset of puberty. In two community-based studies, clinically-diagnosed acne was identified in 29% of Taiwanese schoolchildren aged 9–11 years and 28% of Australian schoolchildren aged 10–12 years, respectively.<sup>9,10</sup>

#### Disease burden

Acne can adversely affect quality of life, due to psychological and emotional distress, including poor self-esteem, social anxiety, depression, and suicidal ideation.<sup>11–16</sup> Data on acne from the Global Burden of Disease study 2010 demonstrated that acne-associated disease burden is considerable and continues to grow.<sup>17,18</sup> In terms of economic burden, a 2006 study estimated the cost of acne to the US economy at >\$US3 billion annually in the form of direct medical costs and indirect costs associated with treatment and lost productivity.<sup>19</sup> These observations suggest an unmet need for acne information, education, and treatments that provide the best patient outcomes.

#### Pathogenesis

Acne is thought to have a multifactorial pathogenesis involving the following interactions:<sup>2,20,21</sup>

1. Hyperkeratinisation of the pilosebaceous unit.
2. Hormonally-induced surplus of sebum production.
3. Presence of the commensal bacterium *Propionibacterium acnes*.
4. An inflammatory immune response.

There is also evidence that neuroendocrine regulation, diet, and genetic and non-genetic factors can contribute to the pathogenesis of acne.<sup>22</sup>

Recent research indicates a more prominent role for inflammation in the pathogenesis of acne than previously thought, with inflammation being present in all acne lesions and potentially at the earliest



stages of lesion development.<sup>20,21,23</sup> Indeed, it has been suggested that inflammation of the pilosebaceous unit should be considered the defining feature of acne.<sup>20</sup>

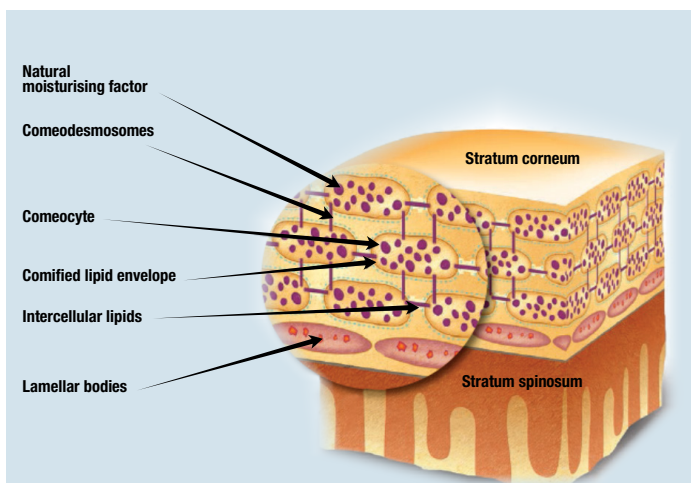
Inflammation as the dominant process in the pathogenesis of acne may require modification of treatment strategies for acne, with more emphasis on agents that have anti-inflammatory properties and less on those with anti-microbial properties.<sup>20,24</sup>

### Effects of disease on the stratum corneum

The stratum corneum (SC) is the outermost layer of the epidermis and its main biological functions are to:<sup>25-27</sup>

1. Provide a barrier to protect underlying epidermal layers and tissue from environmental insult.
2. Prevent excessive water loss, measured as transepidermal water loss (TEWL).

The SC is composed of corneocytes surrounded by a continuous phase of lipids (**Figure 1**).<sup>28,29</sup> The corneocytes are held together by protein structures called corneodesmosomes and to maintain their hydration the corneocytes produce natural moisturising factor. The continuous lipid phase is a mixture of ceramides, cholesterol, and free fatty acids, which are produced by the lamellar bodies. Together with the hydrophobic cornified lipid envelope, the intercellular lipids maintain the moisture balance within the SC. The structural and functional integrity of the SC is highly dependent on adequate water content.



**Figure 1.** The structure of the stratum corneum and its components.

Inflammatory skin diseases, including acne, have been associated with impairment of the SC, including its lipid composition and biosynthesis.<sup>25,26,30,31</sup>

There is some evidence that acne is associated with an inherent structural and/or functional impairment of the skin barrier.<sup>26,31</sup> The skin of patients with mild to moderate acne has been demonstrated to have higher TEWL, lower water content (hydration), and reduced ceramide content compared with control subjects.<sup>32</sup> These observations support an association of SC permeability barrier impairment with acne. Reduced amounts of ceramide in the SC associated with impaired water-barrier function of the skin has also been demonstrated in atopic dermatitis.<sup>33</sup>

### Risk factors

The following factors may contribute to the development of acne or exacerbate existing acne:<sup>2,34</sup>

- Increased androgen hormone levels in some female acne patients, e.g. polycystic ovarian syndrome.
- Medications, such as corticosteroids, anabolic steroids, anti-epileptic agents, or lithium.
- Exposure to oils (cosmetic or occupational).
- Excessive humidity.
- Friction or pressure on the skin caused by helmets, headbands, tight collars, and backpacks.
- Diet, although previously thought to be a myth, does have a role in influencing acne. Eating food with a high glycaemic index may worsen acne.
- Stress may exacerbate acne through hormonal influences (increased sebum production).

Making lifestyle changes based on the above risk factors may help to control acne, e.g. minimise stress, stop smoking, eat a balanced low-glycaemic diet, avoiding friction and/or pressure on the skin.<sup>35,36</sup>

### Diagnosis

The diagnosis of acne is based on clinical assessment.<sup>1,2</sup> The typical signs and symptoms of acne include the following:

- Oily skin due to increased sebum production (seborrhoea).
- Closed comedones (whiteheads).
- Open comedones (blackheads).
- Erythematous papules (tender small red bumps).
- Pustules (white/yellow spots).
- Deep inflamed nodules (large solid painful lumps beneath the skin surface).
- Cysts (painful, pus-filled lumps beneath the skin surface).
- Severe acne may result in hyperpigmentation in darker skin and scarring.

The areas that are most frequently affected have the highest density of sebaceous follicles, i.e. the face, neck, back, and chest.<sup>2</sup>

Often, acne severity is generically referred to as mild, moderate, or severe, based on the number, type, and distribution of lesions. Lesions can be inflammatory or non-inflammatory.

### Treatment

In current published international management guidelines, treatment depends on the severity of acne, with or without the specific consideration of lesion type.<sup>22,37,38</sup> The American Academy of Dermatology guidelines, for example, clearly defines specific first-line treatments for mild, moderate, and severe acne (**Table 1**).<sup>22</sup>

Clinical treatment algorithms vary across different guidelines but the general principles are:<sup>22,37,38</sup>

- Combination topical therapy should be used in the majority of patients.
- Topical formulations of benzoyl peroxide, antibiotics (e.g. clindamycin and erythromycin) combined with a retinoid (e.g. adapalene, tretinoin) are recommended for acne that is of mild severity.
- Oral antibiotics (e.g. tetracycline) are recommended for moderate and severe acne and acne that has not responded to topical therapy. Oral antibiotics should be used in combination with a topical retinoid and/or benzoyl peroxide.
- Oral isotretinoin is recommended for severe acne and acne that has not responded to topical or oral therapy.



A combination of topical retinoid and antimicrobial therapy is generally recommended as first-line therapy for most patients with acne. Combination therapy achieves superior efficacy versus monotherapy via complementary mechanisms of action targeting different pathogenic factors involved in acne.<sup>39</sup> Retinoids act by having comedolytic and anti-inflammatory effects. Benzoyl peroxide is antimicrobial with some keratolytic effects. Antibiotics exert antimicrobial and anti-inflammatory effects.

Other relevant recommendations and considerations of current guidelines include the following:<sup>22,37,38</sup>

- Topical and systemic antibiotics are not recommended as monotherapy (to reduce the risk of bacterial resistance).
- Topical azelaic acid is a useful adjunctive treatment.
- Oestrogen-containing combined oral contraceptives are effective in the treatment of inflammatory acne in females.
- Spironolactone may be useful in the treatment of acne in certain female patients.
- Isotretinoin has many adverse effects, is a teratogen, and requires monitoring. Therefore, isotretinoin should only be prescribed by physicians educated in its use, patients should receive extensive instruction about the drug, and strict precautions for pregnancy must be followed.

There is limited evidence to recommend the use of physical modalities for the routine treatment of acne, such as light and laser therapies or chemical peel.<sup>22</sup> However, these therapies may be of benefit in patients unable to tolerate or who do not respond to medical therapies.<sup>38</sup>

Limited low-quality evidence indicates that tea tree oil may reduce total skin lesions in acne.<sup>22,40</sup> There is a lack of evidence to support the use of other complementary or alternative medicines for the treatment of acne. It should also be noted that there is a potential for adverse effects from herbal medicines.<sup>40</sup>

Mild	Moderate	Severe
Benzoyl peroxide (BP) or Topical retinoid	Topical Combination Therapy**	Oral Antibiotic +
-or-	BP + Antibiotic or Retinoid + BP or Retinoid + BP + Antibiotic	Topical Combination Therapy**
Topical combination therapy**	-or-	BP or Retinoid + BP
BP + Antibiotic or Retinoid + BP or Retinoid + BP + Antibiotic	Oral Antibiotic + Topical Retinoid + BP	-or-
	-or-	Oral Isotretinoin
	Oral Antibiotic + Topical Retinoid + BP + Topical Antibiotic	

**Table 1.** Algorithm for the first-line treatment of acne according to acne severity as recommended by the American Academy of Dermatology.<sup>22</sup>

\*\*Drug may be prescribed as a fixed combination product or as a single agent. Abbreviation: BP = benzoyl peroxide.

Optimal management of acne should involve patient education, a rational and individualised therapeutic regimen, and integration of proper skin care.<sup>41</sup> A gentle daily skin care regimen is important to support any acne treatment plan.<sup>36,38</sup>

## Adherence to treatment

A successful clinical outcome requires that patients stick to their treatment plan.<sup>15,42</sup> Factors likely to contribute to poor adherence include:

- Incomplete or slow response to therapy.
- Side effects from treatment, such as skin irritation or dryness.
- Regimens that are too complicated and/or inconvenient.

The rate of poor adherence was 50% in a validated questionnaire that assessed adherence to acne treatment in a large multinational group of acne patients.<sup>42</sup> Poor adherence was more common in patients using a combination of systemic and topical therapy (60%) than in patients treated with topical therapy only (40%). Young age, side effects, lack of clinical improvement, lack of knowledge about acne treatment, and lack of patient satisfaction with treatment were correlated with poor adherence. Factors that had a positive effect on adherence included severe acne, use of moisturisers and cleansers, clinical improvement, satisfaction with therapy, and knowledge of acne treatment.

Studies show that using moisturisers helps acne treatment by increasing adherence, including treatment with a topical retinoid.<sup>42,43</sup>

According to a survey of young acne patients receiving topical therapy with a fixed-combination product (clindamycin/benzoyl peroxide), bothersome side effects included dry skin (55%), flaky/peeling skin (45%), irritated skin (44%), itchy skin (39%), and redness (37%).<sup>44</sup> Consequently, the product was used only as a spot treatment (33% of patients), only when breakouts seemed worse (28%), or less often than recommended (32%). Some patients stopped using the product from time to time (32%) and some stopped using it altogether (10%). Notably, 41% of subjects reported using moisturisers to counteract dryness and redness.

Educating patients about their acne, medication, and skin care is recommended to improve adherence.<sup>10,38</sup>

### PRACTICE TIPS 1: CORRECT USE OF ACNE MEDICATIONS

To get maximum benefit from acne medications, patients should be advised that:

- Topical medications should be applied:
  - to clean, dry skin.
  - as a thin smear to the area that is prone to acne, ideally the whole face
  - spot treatment of individual pimples is less effective.
- Topical medications may lead to dryness, which will improve as the skin 'acclimatises' to the medication (about 2-3 weeks).
- Medication-induced dryness can be minimised by:
  - waiting 15–20 minutes after washing before applying topical medication.
  - starting by applying every 2 or 3 days, gradually working up to daily use.
  - adjunctive use of a moisturiser.
- Patience is required! Medications should be used as directed for  $\geq 6$  weeks. Topical treatments prevent the formation of new lesions and it takes time for existing lesions to heal.
- Persistence is required! Medication use should not be stopped just because the acne is better. Acne is a chronic condition and the primary effect of treatment is to prevent the development of new lesions.
- Planning pregnancy, pregnancy, and breastfeeding may require a change in the treatments prescribed so consultation with their doctor may be needed.



## Skin care

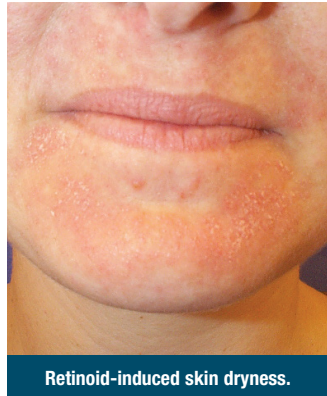
The use of a gentle cleanser and moisturiser may be beneficial in skin diseases where epidermal barrier function is impaired.<sup>26,45,46</sup>

Twice daily use of a gentle cleanser in patients with mild or moderate acne has been shown to reduce acne lesion counts in clinical studies,<sup>47-49</sup> and not to damage the skin barrier or result in sebum overcompensation.<sup>50</sup> In another study, the combined use of a gentle facial skin cleanser and moisturiser in patients with mild acne and dry skin was associated with a reduction in acne and the improvement of dry skin, with increased levels of endogenous ceramide in the SC being observed.<sup>51</sup>

## Skin care as an adjunct to treatment

Skin care as an adjunct to medical-based regimens has the potential to reduce local irritant reactions resulting from the use of topical treatment.<sup>26,45,46</sup>

The mainstay acne treatments benzoyl peroxide and topical retinoids are associated with irritant contact dermatitis, occurring with erythema, burning, dryness, scaling, and itching.<sup>26,52,53</sup> For example, a nearly 2-fold increase in TEWL has been demonstrated with sequential application of benzoyl peroxide to human skin.<sup>54</sup> With topical retinoids there is often an initial period during which the skin acclimates to the drug, which is characterised by peeling, flaking, and erythema ('retinoid dermatitis').<sup>26</sup> The potential for topical acne medications to impair the SC permeability barrier is a well-known side effect of topical treatment.



## Adjunctive moisturiser

Regular use of moisturiser as an adjunct to topical tretinoin monotherapy has been shown to facilitate the skin's adaptation to retinoids in patients with acne, as evidenced by improvements in skin dryness, roughness, and desquamation,<sup>55</sup> and in patients with photodamaged skin, as evidenced by signs of reduced cutaneous irritation and decreased TEWL.<sup>56</sup>

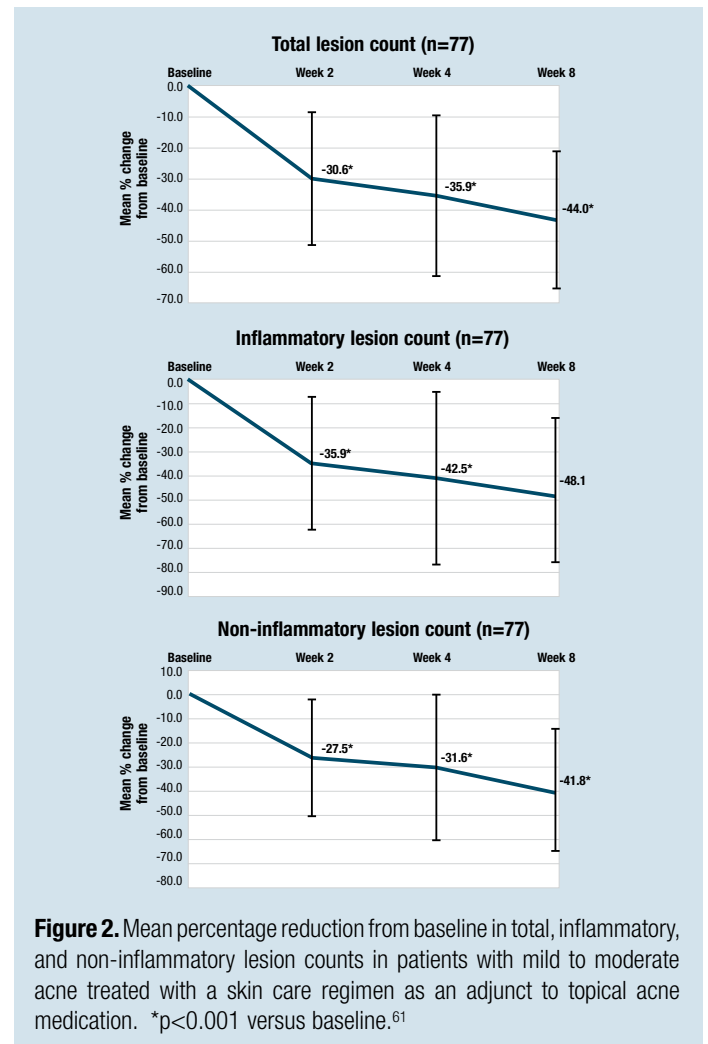
In another study, adjunctive use of moisturiser in acne patients treated with the combination regimen of adapalene and clindamycin for four weeks was associated with significantly ( $p < 0.05$ ) increased water content in the SC and reduced sensation of dryness versus no moisturiser.<sup>57</sup> Importantly, moisturiser use did not affect the efficacy of the topical acne treatment, which produced a significant reduction in inflammatory ( $p < 0.05$ ) and non-inflammatory ( $p < 0.01$ ) lesion counts. This finding is confirmed by a study in which moisturiser use facilitated the efficacy and tolerability of a triple-combination regimen comprising tretinoin, benzoyl peroxide, and clindamycin in the treatment of facial acne.<sup>58</sup>

Another factor informing skin care for patients with acne is that topical retinoids, tetracyclines, and benzoyl peroxide can predispose patients to photosensitivity, which can be improved by use of sunscreen.<sup>59,60</sup>

## Adjunctive cleanser, moisturiser, and sunscreen

An open-label observational study, designed to mirror the treatment of facial acne vulgaris in clinical practice, evaluated the efficacy, tolerability, and patient acceptance of a specified skin care regimen as an adjunct to combination topical acne therapy in patients with mild or moderate acne.<sup>61</sup> Patients were treated with topical adapalene/benzoyl peroxide, applied once daily, in conjunction with a branded foam wash, used twice daily, and branded moisturiser SPF30, applied once daily in the morning.

After 8 weeks, there was a significant ( $p < 0.001$ ) reduction in total, inflammatory, and non-inflammatory lesion count (**Figure 2**).<sup>61</sup> The combination regimen was well tolerated, well accepted, and adherence was high (94%). At the end of the study, most of the patients (70%) agreed that a moisturiser with sunscreen made for acne-prone skin was important. Less than half of patients (34%) felt that use of a moisturiser with sunscreen was important at the start of the study.



**Figure 2.** Mean percentage reduction from baseline in total, inflammatory, and non-inflammatory lesion counts in patients with mild to moderate acne treated with a skin care regimen as an adjunct to topical acne medication. \* $p < 0.001$  versus baseline.<sup>61</sup>

## PRACTICE TIPS 2: SKIN CARE

Good skin care habits support prescription acne medications, which can be potentially irritating. Patients should be advised to:

- Gently wash their face twice a day, in the morning and in the evening.
- Avoid over-washing/scrubbing as it may lead to skin dryness and irritation.
- Use gentle non-medicated soaps and cleansers.
- Apply non-fragranced non-comedogenic oil-free moisturiser to dry areas of skin.
- Use makeup or sunscreen that is oil-free and non-comedogenic.
- Avoid 'popping pimples' or picking at their acne, as this may lead to scarring or infection.
- Pay attention to how sports equipment (e.g. helmet straps) might rub against the skin.



### Skin care recommendations

A Canadian expert panel found the following:<sup>62</sup>

1. Dry skin and irritation is a primary reason for patient non-adherence to acne treatment.
2. Skin barrier dysfunction may contribute to the signs and symptoms of acne.
3. Topical acne treatment and systemic retinoid therapy often result in dry skin and irritation.
4. Moisturisers can improve dryness and irritation resulting from acne treatment.
5. Ceramide-containing moisturisers may enhance adherence existing acne therapies.

This expert panel proposed that adjunctive therapy with moisturisers, especially ceramide-based moisturisers, should be considered in patients receiving acne treatment.<sup>62</sup>

Other guidelines stress the importance of educating acne patients about cleansing, moisturising, and sun protection. For example, instructions from dermatologists on the use of skin care as an adjunct to standard medical treatment for acne has been shown to have beneficial effects on quality of life in patients with acne.<sup>63</sup>

#### PRACTICE TIPS 3: WHEN TO REFER

Referral to a dermatologist should be considered when there is:

- Diagnostic uncertainty. Is it really acne or rosacea or perioral dermatitis or another differential diagnosis.
- Non-response to medical treatment given for a sufficient period of time, usually 3–6 months.
- Nodular acne or any type of acne with a tendency to scarring.
- Likelihood of post-inflammatory hyperpigmentation, usually moderately severe acne in patients with deeply pigmented skin.
- Major psychological component to the disorder.
- Patient interest in alternative treatments.

#### EXPERT'S COMMENTARY – SUSAN SIMPKIN

It is interesting to note the impaired skin barrier function seen in acne vulgaris, similar to that seen in other inflammatory skin conditions. Treatments for acne including benzoyl peroxide, topical retinoids, and oral isotretinoin can lead to irritant dermatitis or may aggravate pre-existing atopic dermatitis. Tetracyclines and retinoids can also cause photosensitivity and sunburn. The use of appropriate skin cleansers and moisturisers in acne can improve tolerability and compliance to medical treatment. Recommendations would include gentle soap-free cleansers and oil-free non-comedogenic moisturisers and sunscreens.

#### EXPERT'S COMMENTARY – JO-ANN SEE

Acne is a common skin condition affecting most of us in our lifetime. Many patients are confused as they develop acne before being teens and others into their adult years. Acne can be intermittent or chronic and can change in severity thus requiring a different treatment approach according to the clinical pattern. Some lifestyle changes may help; however, skin care and medical management are of utmost importance.

Acne skin can have a compromised epidermal barrier, which may be further impaired as a side effect of acne therapy. Unfortunately, many acne medications can cause skin irritation and dryness, which can be significantly improved with gentle cleansing and moisturising as an adjunct to medical treatment. This will in turn improve patient adherence and outcome.

So, not only does the doctor have to be aware of efficacy and side effect profiles of acne treatments but now must be knowledgeable about good skin care.

#### TAKE-HOME MESSAGES:

- Acne vulgaris is a chronic inflammatory skin condition.
- The prevalence of acne is high, especially in teenage and early adult years.
- Acne also occurs in pre-teens and older adults.
- Acne is associated with adverse psychosocial and physical sequelae.
- Treatment recommendations include:
  - Benzoyl peroxide and a topical retinoid either alone or in combination (with/without a topical antibiotic) for mild acne.
  - Oral antibiotics combined with topical therapy for moderate acne.
  - Oral antibiotics combined with topical therapy or oral isotretinoin for severe acne.
- Poor adherence to treatment is common, partly due to side effects of acne medications, such as skin irritation, or difficult-to-follow treatment plans.
- Acne-affected skin may be associated with impaired skin barrier function and greater propensity for skin dryness.
- Some acne medications may impair SC function potentially leading to skin inflammation and dryness.
- Gentle cleansers and moisturisers, as an adjunct to acne medication, can improve skin condition, which may improve treatment adherence.
- Patients should be referred to dermatologist when treatment goals are not met.



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