# Acne Vulgaris in Skin of Color: Understanding Nuances and Optimizing Treatment Outcomes

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## ABSTRACT

According to the United States national survey data, acne vulgaris is the leading dermatologic diagnosis among African Americans, Hispanics/Latinos, and Asians/Pacific Islanders. This patient population, collectively referred to as having skin of color, exhibits clinical and therapeutic nuances that are relevant in the management of acne. Understanding the nuances in clinical presentation, safety considerations, cultural factors, and desired treatment endpoints is key to ensuring successful outcomes.

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## INTRODUCTION

### Epidemiology

Published practice and community-based survey studies have reported that acne is the most frequent dermatologic condition in populations with skin of color, including blacks (in New York, NY;[1] Washington, DC;[2] and London, UK[3]), Latinos (in New York, NY),[4] Arab-Americans (in Southeast Michigan),[5] and South-Asian Americans (in New York, NY).[6] In a global study, unilateral facial photographs of 2,835 females (10 to 70 years of age) from 4 cities (Los Angeles, USA; London, UK; Akita, Japan; and Rome, Italy) were examined for clinical features of acne. The prevalence of acne was found to be 37%, 32%, 30%, 24%, and 23% in African Americans, Hispanics, Asians, Caucasians, and Continental Indians, respectively.[7]

### Clinical Nuances

Increased constitutive pigmentation and labile melanocyte responses to inflammation are key characteristics of skin of color. As a result, inflammatory disorders of the skin, such as acne, are typically complicated by the presence of postinflammatory hyperpigmentation (PIH). Acne-associated PIH is characterized by hyperpigmented macules typically ranging from 2 mm to 4 mm in size arising at sites of resolved or resolving acne lesions (Figure 1). Although spontaneous remission is expected, PIH generally lasts from several weeks to several months after an acne lesion has resolved, depending on the severity.

Patients frequently refer to PIH as "uneven skin tone" or "acne scars," and may have the misconception that the lesions are permanent if left untreated. In many instances, PIH is of greater concern to the patient than the acne itself; it is often the driving force for acne patients with skin of color to seek a dermatologist consultation. In the setting of excoriation or other traumatic manipulation of acne lesions by the patient, PIH tends to be more severe and longer lasting (Figure 2). A harsh skin care regimen (eg, vigorous scrubbing, or excessive use of exfoliating products, strong toners, or astringents, etc) can also contribute to PIH. In cases of severe excoriation or "acne excoriée," hypopigmented macules with angulated hyperpigmented borders can be observed (Figure 3).

Populations with skin of color (especially those of sub-Saharan African ancestry) have a higher prevalence of keloids and hypertrophic scars.[8] This is due to a genetic predisposition toward heightened fibroblast responses to injury and inflammation. Inflammation from acne, particularly in cases of severe truncal involvement, can therefore lead to the formation of keloids in individuals who are so predisposed. As such, moderate to severe acne in populations with skin of color is associated with a higher risk of disfiguring and persistent raised scars, which are most frequently observed on the chest, upper back, and jawline.

There are a number of cultural skin and hair care practices that can in some instances exacerbate acne.[9] One example is the more frequent use of cocoa butter lotions and creams among African Americans.[10] This is due to a widely held perception in this population that cocoa butter helps to even skin tone and improve scars. Therefore, in an effort to reduce the hyperpigmentation and perceived "scars" of PIH, many patients with skin of color (particularly African Americans) may apply cocoa butter liberally to the face. This in turn can exacerbate acne due to its comedogenicity.

Another cultural practice that can contribute to worsening acne is the frequent use of thick, oil-based hair products among populations of African ancestry with afro-textured hair. In this population, the application of hair products designed to add sheen, prevent dryness, and improve manageability is a common practice. Historically, thicker products containing petrolatum or mineral oil have been used and these have

**FIGURE 1.** Acne and associated postinflammatory hyperpigmentation.

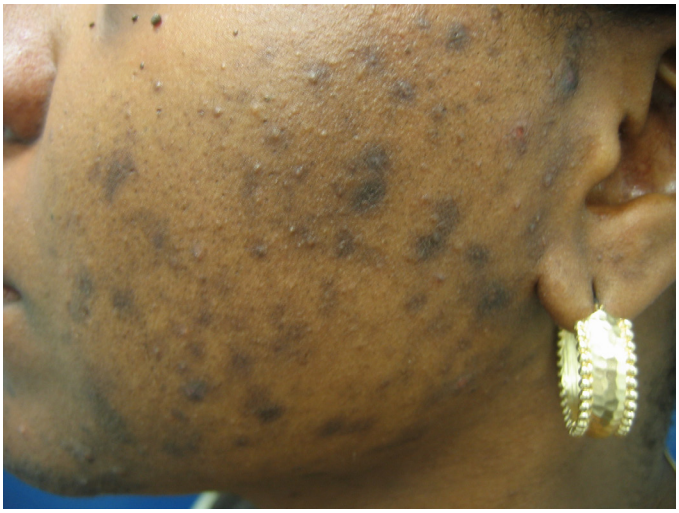
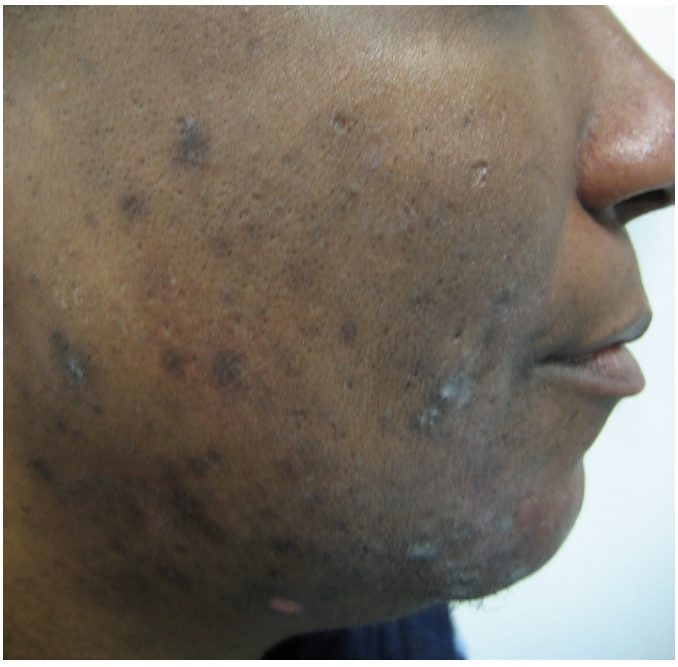


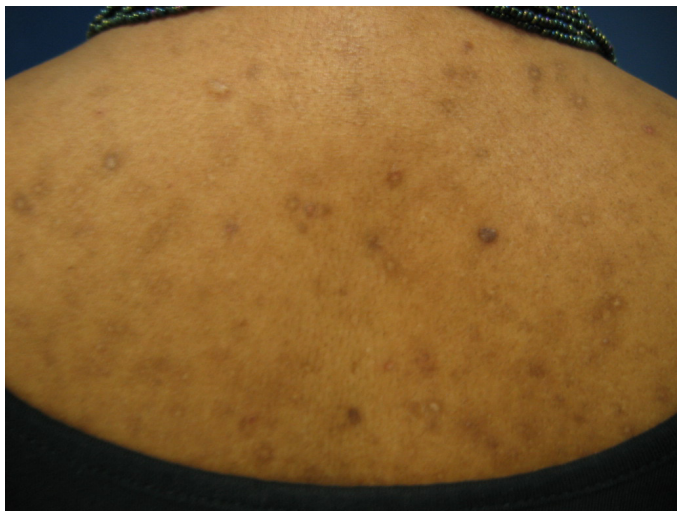
**FIGURE 2.** Acne with excoriation.



been associated with pomade acne.[11] This variant of acne is less common today than when it was first described over 4 decades ago due to shifts in consumer preferences toward lighter, less greasy hair products. However, it can still be observed and, when it is identified, patients should be counseled on using alternative hair products that are less likely to cause acne, such as silicone-based hair serums (containing cyclomethicone or dimethicone).[9,12]

The use of over-the-counter topical skin lightening or skin bleaching creams is not uncommon among patients with skin of color, many of whom try such products as a treatment of

**FIGURE 3.** Acne excoriée with hypopigmented macules and hyperpigmented borders.



PIH and other dyschromias before seeking a dermatology consultation.[9] In addition to hydroquinone-based products, some skin lightening creams sold at ethnic beauty supply stores and via the internet illegally contain prescription-strength corticosteroids, such as clobetasol and bethamethasone valerate.[13] As such, steroid acne can be seen in this context. Clinical clues to this diagnosis include an acute flare of acne with monomorphous inflamed papules and pustules in association with facial hypopigmentation and atrophy. Patients are generally unaware that such bleaching creams may contain potent corticosteroids and often do not consider mentioning these products to their physician unless asked directly. Therefore, the diagnosis rests on the dermatologist having a clinical suspicion when presented with the aforementioned signs and symptoms. Requesting that the patient bring in all their skin care products is a useful way to detect the inadvertent long-term use of corticosteroids on the face, or other products that may contribute to acne.

## The Role of Inflammation

It has been well established that inflammation plays an integral role in the pathogenesis of acne, particularly in the context of papules, pustules, nodules, and "cysts." However, only recently has the role of inflammation as an early and subclinical event in the development of acne been elucidated.

In a 1996 study, Halder et al[14] examined 30 black females with acne, obtaining punch biopsies of lesional skin. Histopathological signs of inflammation were found to be out of proportion to clinical inflammation and extended beyond the boundaries of clinically inflamed lesions. Moreover, even clinically non-inflamed lesions (ie, comedones) exhibited inflammation histopathologically. This subclinical inflammation likely contributes to the high propensity toward PIH in acne patients with darker skin (including those with mild to moderate acne).

However, more recent evidence supports the notion that subclinical inflammation is not unique to skin of color, but rather a pathogenic feature of acne in general. In an immunohistochemical study examining biopsies of clinically normal perifollicular skin, clinically inflamed acne lesions, and control samples from subjects without acne, Jeremy et al[15] found that levels of interlekin-1 (a proinflammtory cytokine) were upregulated in perifollicular skin. In addition, numbers of CD3+, CD4+ T-lymphocytes were increased in perifollicular skin compared with controls.[15] Taken together, inflammatory responses may be a primary event in the pathogenesis of acne and can precede the development of clinically detectable acne lesions.

Subclinical inflammation in acne is of particular importance to skin of color given the risk of postinflammatory pigment alteration. Inflammatory mediators including prostaglandins and leukotrienes have been shown to stimulate melanocyte pigment production.[16] Therefore, it is plausible that effective control of inflammation (both clinical and subclinical) may reduce the severity and number of hyperpigmented macules associated with acne in skin of color.

An important driver of inflammatory responses associated with acne is the bacterium, *Propionibacterium acnes*. There is evidence that *P. acnes* activates innate immunity via toll-like receptor 2 (TLR-2) leading to release of interleulin (IL)-1α from keratinocytes, which in turn stimulates follicular hyperkeratinization and the formation of the microcomedo.[17] It has recently been shown that *P. acnes* activates inflammasomes leading to the production of IL-1β by monocytes, which could contribute to increased inflammation.[17,18] Targeting *P. acnes* is therefore a core strategy in the management of acne and its associated inflammatory responses.

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## Implications for Treatment

The greater tendency toward dyspigmentation and keloid scarring in patients with skin of color has important therapeutic implications.

1. Early and aggressive control of acne-associated inflammation is imperative. This can be accomplished with the use of a well-rounded treatment regimen that targets multiple factors in the pathogenesis of the disease and includes agents with anti-inflammatory properties. Acne treatments with anti-inflammatory effects include topical retinoids, the oral tetracycline antibiotics, topical dapsone, and azelaic acid. Among the retinoids, the anti-inflammatory activity of adapalene has been the most studied. Adapalene has been shown in vitro and in vivo to decrease expression of toll-like receptor (TLR)-2 (a receptor of the innate immune system) and IL-10 (an anti-inflammatory cytokine). (Zuliani T et al. *Exp Dermatol*. 2011;20:850-853.) In addition, adapalene increases expression of CD1d – a cell surface glycoprotein that plays a role in antigen presentation and induction of cutaneous inflammatory responses. Other anti-inflammatory effects of adapalene include inhibition of arachadonic acid metabolism, neutrophil chemotaxis, and free radical production.[19] Benzoyl peroxide (BPO), through its microbicidal effects, indirectly reduces inflammation by killing *P. acnes* – a trigger of acne-associated inflammation.

   A well rounded regimen includes a multi-pronged approach to address the multiple pathogenic factors associated with acne, including follicular hyperkeratinization, *P. acnes* inflammation, and increased sebum production. Therefore, combination topical regimens that include a topical retinoid, a BPO, and/or an immunomodulating agent (eg, dapsone, azelaic acid) tend to be the most effective.

   Under-treatment of acne in patients with skin of color should be avoided, given the greater risk of dyspigmentation and keloidal scarring (in more severe cases). As such, the threshold for using oral antibiotics (for their anti-inflammatory and anti-*P. acnes* effects) in the appropriate patient is low. Regimens that initially include oral doxycycline or minocycline in combination with a topical retinoid followed by maintenance with a topical retinoid is a well-established long-term treatment strategy in the general acne population,[20,21] and is particularly well suited to patients with skin of color.

   Oral isotretinoin should also be considered for the appropriate patient with severe inflammatory acne who is at risk for scarring, as well as for patients who fail oral antibiotics. It has been reported based on U.S. National Ambulatory Medical Care Survey data that isotretinoin is less frequently prescribed to blacks than to whites; cost may contribute to this disparity, but patient and provider biases as well as racial differences in severity cannot be ruled out.[22] When warranted, oral isotretinoin should be considered early in the course of nodulocystic or other severe forms of acne in patients with skin of color.

   In cases of severely inflamed papules or nodulocystic lesions, the use of intralesional corticosteroid injections (typically triamcinolone acetonide 2.5 mg/mL to 3.3. mg/mL) to rapidly reduce local inflammation is an effective

short-term measure. However, overly aggressive intralesional injections using higher concentrations can lead to corticosteroid-induced hypopigmentation in darker skinned patients.

2. Avoiding iatrogenic PIH from medication-induced irritation is essential. Special considerations need to be made regarding specific therapeutic agents, concentrations, and vehicles in order to select a regimen that is well tolerated by a given patient. While all Food and Drug Administration (FDA)-approved topical acne treatments can safely be used in patients with skin of color, individual variations in sensitivity exist and should be accounted for when selecting a regimen for any given patient. Erring on the side of increased tolerability is a prudent approach for patients with skin of color, given that any irritant reactions can lead to pigmentary alterations (hyper- or hypo-pigmentation). While such treatment-related dyschromias are generally self-limited, they tend to cause considerable patient anxiety and loss of confidence in the prescriber on the part of the patient.

   Tolerability considerations are especially important when selecting topical retinoids. While all FDA-approved topical retinoids can safely be used in patients with skin of color, adapalene 0.1% is associated with the least irritation potential[23-26] and has been studied in numerous populations with skin of color – including studies conducted in South Africa,[27,28] Japan,[29] China,[25] Singapore,[26] and Mexico.[30] Tretinoin is best tolerated in a branded microsphere formulation or an aqueous gel. However, when generic tretinoin formulations are used, it is advisable to initiate treatment with the lowest concentration (0.025%), titrating up to higher concentrations in the appropriate patient.[10] Tazoratene is best tolerated as a cream; initiating this at the lowest concentration (0.05%) and titrating to higher concentrations and/or gel formulations in the appropriate patient is the preferred approach.[10]

   When BPOs are used on the face, vehicle and concentration considerations are important with respect to maximizing tolerability. When treating facial acne, 2.5%-5.5% BPO formulations in aqueous gels, microsphere cream, or emollient foam are generally well tolerated and strongly preferred over products in ethanolic gels or those with higher concentrations. However, concentrations up to 10% found in BPO cleansers or a short-contact emollient foam preparation are generally well tolerated on the trunk.

   Several meta-analysis studies investigating the comparative safety and efficacy of topical acne formulations between higher and lower Fitzpatrick skin types, as well as investigations into specific racial/ethnic groups, have recently been published. Most recently, a subgroup analysis evaluating the efficacy and safety of adapalene 0.1%/BPO 2.5% gel in 238 black subjects was published. Adapalene/BPO gel was well tolerated in this cohort, and no cases of treatment related PIH were observed.[31] A previous study demonstrated comparable tolerability of adapalene/BPO gel in subjects with Fitzpatrick skin types I to III and IV to VI.[32] A similar study involving clindamycin phosphate 1.2%/BP gel found no differences in cutaneous irritation in Fitzpatrick skin types I to III vs IV to VI.[33] This formulation was also investigated in Hispanic subjects in a post-hoc analysis, in which Hispanic patients were not found to be more sensitive to treatment-related cutaneous irritation. A small pilot study found clindamycin phosphate 1.2% and tretinoin 0.025% gel to be well tolerated in 33 patients with Fitzpatrick skin types IV to VI.[34] In a subset analysis of a community-based trial of combination therapy with clindamycin 1%/BPO 5% gel and topical tretinoin microsphere or adapalene gel 0.1%, treatment was well tolerated with a trend toward better resolution of hyperpigmentation with clindamycin/BPO gel in combination with tretinoin microspere gel 0.04%.[35] In a comparative meta-analysis, adapalene 0.1% in black patients vs white patients was associated with a low incidence of irritation (erythema, scaling, and dryness).

   To maximize tolerability, patients should be counseled to avoid harsh scrubs, toners, and exfoliating cleansing routines that can increase the risk of irritation from prescription therapies.[36] Initiating therapy with every other night dosing of retinoids and applying a non-comedogenic moisturizer immediately after topical prescriptions are useful strategies for maximizing tolerability and minimizing dryness/peeling. In patients with extremely dry, sensitive skin, applying a moisturizer prior to the retinoid can be helpful.[37]

3. Designing a treatment regimen that helps to reduce PIH is a strategy that increases patient satisfaction. This involves selecting products that have dual efficacy–treating both acne and hyperpigmentation (such as retinoids and azelaic acid), as well as adjunctive therapies that specifically target PIH (including hydroquinone and chemical peels).[9,38] The topical retinoids are particularly useful in the management of both acne and PIH in skin of color. Tretinoin,[39] adapalene,[27,28] and tazarotene[40] have all been shown to reduce PIH in studies involving patients with skin of color. A fixed dose of triple combination therapy has also been shown to improve PIH. (Galderma data on file, study report HDTL 043 A-B). To align the dermatologist's treatment endpoint with patient expectations, follow-up evaluations should be continued until the clearance of both active acne lesions and PIH. Thus, the time course to achieving a treatment success is on average longer in a patient with skin of color, typically spanning 6 months or more.

4. Identifying and eliminating potentially exacerbating factors that are more prevalent in specific populations (discussed above) is an important step toward ensuring favorable treatment outcomes.

## CONCLUSION

The treatment of acne in skin of color patients involves selecting a regimen that ensures early and sustained control of inflammation; avoidance of irritation to prevent iatrogenic dyspigmentation; treatment of both acne lesions and associated PIH; and identification of potential cultural factors that can exacerbate or contribute to acne.

## DISCLOSURES

Andrew F. Alexis MD MPH has served as a consultant for Galderma, Allergan, Estée Lauder, Johnson & Johnson Consumer Companies Inc, L'Oréal, and SkinMedica.

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