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ACNE IN ETHNIC SKIN: CONSIDERATIONS FOR POSITIVE TREATMENT OUTCOMES

Here, Dr. Jennifer Linder reviews what doctors need to know to treat acne in ethnic skin.

JENNIFER LINDER, MD



Photo courtesy PCA SKIN.

Experts estimate that the majority of the U.S. population in the 21st century will have skin of color.¹ This, combined with the reality that acne is believed to be the most prevalent skin condition in all Fitzpatrick skin types,² (Table I) makes it critical to understand the cutaneous histological variances that exist in patients of color with acne.

BEYOND SKIN COLOR

To best serve one's patients, it is important to understand acne in ethnic skin. A patient's heredity should be considered when developing a treatment plan for any skin condition. It is clear that color is only one of the im-

portant differences in the range of skin hues. By defining the key predispositions of ethnic skin, we can identify the complex and unique needs of each patient's skin and, thereby, create successful treatment pathways.

Acne therapy can be particularly difficult in darkly pigmented individuals, as the acne lesions themselves and the aggressive products often used to treat breakouts frequently result in post-inflammatory hyperpigmentation. Using gentle and effective exfoliation methods as well as products to control sebum, inflammation and bacteria will contribute to faster, more consistent results while minimizing potential side effects.

EPIDERMAL AND DERMAL VARIANCES BETWEEN ETHNICITIES

The physiological differences between racial groups, though small, make a significant difference in determining one's propensity toward specific skin conditions. The variability in skin thickness, barrier function, sebaceous and eccrine gland activity, and the melanogenesis and inflammatory response can significantly affect treatment outcome.

Epidermal variations include differences in the stratum corneum (SC). One study showed that the African-American SC contains approximately 22 layers, while that of Caucasian skin has only 17.³ The epidermal thickness,



Figure 1. Before (left) and After (right) 12 weeks of using these products: lactic acid-based facial cleanser; 2% hydroquinone, kojic acid and azelaic acid spot treatment; 0.5% retinol serum; arbutin and birch anti-inflammatory cream; broad-spectrum SPF 30 daytime moisturizer; and aloe vera-based, anti-inflammatory evening hydrator. (No professional treatments were administered.) Photos courtesy PCA SKIN.

Using topical ingredients capable of reducing bacteria, inflammation and the production of melanin will dramatically limit the length of treatment when used independently or in concert with a short course of oral or topical antibiotics. There are several natural and synthetically produced topical agents that perform multiple functions within the skin.

- **Azelaic acid** is used in the treatment of many dermatological conditions, such as acne, rosacea and hyperpigmentation. Studies demonstrate antibacterial and anti-inflammatory properties, keratolytic action and selective cytotoxic effects on epidermal melanocytes.²²⁻²³ Research has indicated that follicular bacterial content is reduced by up to 97% after three months of daily use.²⁴ Azelaic acid is unique in that its bactericidal benefits are not affected by bacterial resistance, and it has less topical irritant potential than benzoyl peroxide (BPO).²⁵ In addition, azelaic acid decreases cellular oxidation, which may explain its anti-inflammatory capabilities.²⁶ The multifunctional activity of this topical ingredient makes it particularly efficacious for treating acne in patients of color.

- **Kojic acid's** antibacterial and copper-chelating capabilities make it an excellent choice for ethnic skin with acne. This fungi-derived ingredient is typically used in pigment control formulations.^{27,28} Its antimicrobial properties make it effective in the clearing of current acne lesions and preventing the formation of PIH.²⁹ There is a potential for contact dermatitis following kojic acid application; therefore, highly sensitive patients should be patch-tested to ensure no undue inflammation is caused during treatment.³⁰

- **Lactic acid** is a hydrophilic alpha hydroxy acid (AHA) that reduces comedo formation by inducing desquamation within the skin while also reducing bacterial colonization and inhibiting the formation of tyrosinase during the melanogenesis process.^{31,32} Lower concentrations up to 5% are recommended for daily use to promote microscopic exfoliation of the corneocytes without causing sensitization or visible flaking³³. Lactic acid also assists in increasing the water content of the epidermis, due to its humectant properties.³⁴

- **Glycyrrhiza glabra** (licorice) root extract is a botanically derived topical agent that provides anti-inflammatory benefits similar to a mild cortisone³⁵ and inhibits lipase, an enzyme produced by the acne bacteria that causes local irritation³⁶. Licorice is also an effective tyrosinase inhibitor, making it incredibly helpful in the clearance and prevention of acne-induced PIH.³⁷

- **Retinoids** include all members of the vitamin A family, including retinoic acid and its analogues (eg, retinol, adapalene, tazarotene, etc.). Retinoids are among the most important ingredients in the management of acne, as they are capable of normalizing follicular keratinization, reducing SC thickness and inflammation.³⁸ Additionally, retinoids assist in the reduction and hindrance of hyperpigmentation by inhibiting tyrosinase, enhancing cell turnover and limiting melanosomal phagocytosis.³⁹⁻⁴¹ While most retinoids are beneficial, I often prefer retinol over retinoic acid for ethnic skin types because of the irritant potential of pure retinoic acid.⁴² Retinol is successfully converted to retinoic acid within the skin, with an approximate 10-fold conversion ratio (eg, 1% retinol is converted to 0.1% retinoic acid).⁴³ The use of retinol makes it possible to achieve similar results to retinoic acid without a heightened irritant risk.

- **Salicylic acid** is used in 0.5% to 2.5% concentrations for at-home acne therapies. Its lipophilic molecule gives it the ability to penetrate through sebaceous plugs and normalize the excess shedding of cells within the follicles.⁴⁴ Topical irritation is minimal with salicylic acid, perhaps as a result of its strong anti-inflammatory properties, making it ideal for darker skin types⁴⁵.

- **Traditional acne therapeutics** such as BPO can and have been used successfully in the treatment of acne in darker complexions. The irritation potential of BPO,^{24,46} however, makes it wise to consider beginning with alternative ingredient options when working with more sensitive ethnic patients.

THE IMPORTANCE OF COMBINATION THERAPY

Combination therapy is also extremely beneficial in the treatment of acne in skin of color. **Exfoliating chemical peeling** treatments should be implemented in conjunction with daily care products to prevent corneocyte adhesion and to rid the skin of excess sebum and bacteria. By reducing SC impaction, the application of peels will also aid in the absorption of other acne control products.

Chemical peels typically are either straight acids in alcohol delivery vehicles or blends of several peeling agents. Peeling solutions that contain higher percentages of a single acid, such as glycolic acid, are more likely to cause inflammation and potentially post-inflammatory hyperpigmentation.⁴⁷ I always recommend beginning the treatment plan cautiously and gradually increase the activity level of the treatment regimen to prevent potential complications. Look for combinations of lower percentages of multiple acids rather than a high percentage of one peeling ingredient. Although more scientific data may be needed, it has been demonstrated that by blending several peeling agents with anti-inflammatory, antioxidant and melanogenesis inhibiting ingredients, the clinician is able to treat the present condition without producing side effects. To minimize complications, it is also wise to limit the depth and aggressiveness of in-office procedures. Although some patients with dark skin may seem quite resilient, it is not about how much discomfort a patient can tolerate. Keeping dark skin calm during treatment is critical to a positive outcome.

AHAs are a group of organic carboxylic acids that dissolve intercorneocyte bonds and encourage desquamation. Each AHA has its own ancillary benefits, and while there are several available, the most common for topical use are lactic and glycolic acids. Lactic and glycolic acids have been utilized for their topical benefits since the late 1970s.⁴⁸ Glycolic acid acts as a strong degreasing agent and assists with



Figure 2. Before (left) and After (right) 12 weeks in which patient received four 20% salicylic acid mask treatments, and used these products: 2% salicylic acid cleanser; 2% salicylic acid and 5% azelaic acid spot treatment; 0.5% retinol serum; broad-spectrum SPF 25 daytime moisturizer; botanical (marigold and cucumber), antibacterial evening hydrator. Photos courtesy PCA Skin.

the over-production of sebum but can be dehydrating to those with a compromised barrier function and drier skin types.⁴⁹ Glycolic acid has the smallest molecular size of all AHA, and its small size leads to quick penetration and epidermolysis.⁵⁰ This fast penetration often induces higher instances of inflammation and stimulation than is associated with other AHA. Lactic acid is typically sourced from sour milk and sugars and is found naturally in human skin. In addition to its exfoliation properties, lactic acid also reduces bacteria,³¹ hydrates the skin³⁴ and fights hyperpigmentation by suppressing the formation of tyrosinase.³² Due to its slightly larger molecule, the amount of inflammation and stimulation associated with lactic acid penetration is relatively small,⁵⁰ making it an ideal option for patients with darker skin tones.

Trichloroacetic acid (TCA) is an excellent peeling agent that has been safely used for more than 80 years.⁵⁰ TCA does not absorb into the bloodstream and works well for ethnic skin when used at lower percentages.⁵¹ At higher percentages, one must be much more cautious, and pretreatment with melanogenesis inhibitors is imperative.⁵² I recommend a series of treatments with blended acid TCA solutions in concentrations up to 10%

for patients of color. There is no downtime associated with these types of treatments. When used in conjunction with lactic acid and antibacterial, anti-inflammatory and anti-dyschromia ingredients, this amount of TCA in a peel offers exfoliation benefits without the risk of over-treatment.

Salicylic acid is a potent anti-acne agent that has been used in the topical treatment of acne since the 1950s.⁴³ This peeling agent also possesses strong anti-inflammatory properties that reduce the chances of developing PIH following treatment.^{53,54} In one study performed on 35 Korean women, 30% salicylic acid peels were effective in the clearing of inflammatory and non-inflammatory acne lesions, and no instances of PIH were reported.⁵⁵ Concentrations of 14% to 20% are also very beneficial with acne patients and are less uncomfortable during treatment.⁵³

CONCLUSION

Every patient is different. A patient's skin color, condition and propensity toward inflammation and heightened melanogenic status should all be considered when developing any treatment plan. The treatment of acne in ethnic skin types requires the utilization of multi-faceted topical in-

Table.

Fitzpatrick Skin Type	Skin Color	Visual Reaction to Sun	Typical Sensitivity to Chemical Peels	Common Response to UV Rays
I	Pale White	Always Burns, Never Tans	Very Resilient	Skin Cancer & Hypopigmentation
II	White	Usually Burns	Resilient	Skin Cancer & Telangiectasia
III	Light Brown, (Naturally Tan) Skin	Mildly Burns, Tans Relatively Well	Moderately Responsive	Telangiectasia
IV	Moderate Brown	Rarely Burns, Tans Well	Sensitive	Hyperpigmentation
V	Dark Brown	Very Rarely Burns, Tans Easily	Moderately Sensitive	Hyperpigmentation
VI	Black	Least Likely to Burn, Tans Very Darkly	Very Sensitive	Hyperpigmentation

however, is similar, suggesting that dark skin may be more compact and prone to cohesion. The presence of a more impacted SC may increase the occurrence and severity of breakouts by trapping sebum and other impurities within the follicle. In addition, transepidermal water loss (TEWL) due to impaired barrier function tends to be greater in African-American, Hispanic and Asian skin.^{1,4,5} This excessive loss of moisture leads to barrier disruption and may result in reduced protection of the nerve endings.⁶ This may explain the heightened sensitivity to topical stimulation that is common in higher Fitzpatrick types.⁷

Dermal differences include a thicker and more compact dermis in skin of color³ and possible distinctions in blood vessels and sebaceous and eccrine glands. Superficial blood vessels are more prominent and dilated in darker skin, although they are typically more visibly apparent in light skin.⁸ The prominence and dilation of superficial blood vessels in darker complexions may play a role in the inflammation associated with acne in darkly pigmented individuals. Some studies suggest that the sebaceous activity in African-American skin is higher than in Caucasian skin due to larger oil glands.⁹⁻¹¹ It should be mentioned that many industry experts consider these trials as flawed and believe more data is needed before determining whether the sebaceous variances between skin tones is significant. Regardless of skin color, over-production of sebum contributes to the formation of acne lesions. Research on eccrine gland activity suggests that it is higher in African Americans

and Hispanics when compared to Caucasians.^{1,11} This natural increase in sweat production may also be a contributing factor to the inflammatory nature of acne in ethnic skin, as perspiration has been shown to create local irritation.¹²

Perhaps the most obvious cutaneous difference between ethnicities is skin color. Although patients of all skin tones have the same number of melanocytes, their function and the quality and distribution of melanosomes are different in ethnic versus Caucasian skin.¹³ The melanogenesis process that leads to the deposition of melanosomes over the nuclei of keratinocytes is identical between races. In skin of color however, the melanosomes are filled with larger melanin granules, which are distributed more evenly throughout the epidermis.^{3,11} The melanocytes themselves are more active and prone to excess and abnormal pigment production.¹⁴ The function and reactivity of melanocytes in darker skin make appropriate treatment selection crucial to avoiding complications and achieving desired results.

ACNE IN ETHNIC SKIN TYPES

Research indicates that acne is among the top three skin concerns in African Americans and those of Latino and Asian backgrounds.¹ Although patients of color are not necessarily more prone to acne than fair-skinned individuals, the residual effects are often much more severe in darker skin. Acne lesions in all ethnicities are a result of reduced desquamation, corneocyte cohesion and the resultant blocked pores, increased sebum production and bacterial proliferation. The type

of lesions seen in various heredities, however, may differ. Grade IV, cystic and nodular acne is more prominent among Caucasians and Latinos than in African Americans.¹⁵ Although the higher grades of acne typically display higher amounts of inflammation than lower grades, comedonal acne in African American skin is much more inflamed than comedonal acne seen in Caucasian skin.¹⁶ Asian and Indian populations seem to be more prone to papular lesions, though the type of acne and severity will vary depending upon exact origin.^{17,18} All of these details are important to take into consideration when creating treatment plans for patients of color.

EFFECTIVE INGREDIENT CHOICES FOR HIGHER FITZPATRICK SKIN TYPES

The key when treating ethnic skin with any skin condition is to limit inflammation. Studies show that melanocytes in higher Fitzpatricks display exaggerated responses to cutaneous inflammation, which explains their propensity toward PIH. In addition, darker skin types have also been shown to release more prostaglandin inflammatory mediators post-trauma, than their lighter counterparts.¹⁹ Pre-treatment with melanogenesis inhibitors, such as hydroquinone, kojic acid and arbutin for several weeks prior to a peel or procedure will assist in the prevention of these potential complications.²⁰ Hydroquinone is potentially irritating at higher percentages.²¹ This irritation could lead to PIH; therefore, I prefer 2% concentrations blended with other, gentler melanogenesis inhibitors for additional benefits without irritation.

redients that are capable of addressing several concerns simultaneously. Comprehensive gentle yet highly effective treatment processes should include daily application of recommended topicals and bi-monthly superficial chemical peels to safely speed patient response and the effectiveness of their treatment. ■

Dr. Linder, a board-certified dermatologist and fellowship-trained Mohs skin cancer surgeon, is a volunteer Clinical Instructor in the Department of Dermatology at the University of California, San Francisco. Dr. Linder is currently in private practice in Scottsdale, AZ.

Disclosure: Dr. Linder is Chief Scientific Officer, PCA SKIN, is National Instructor, Dermik Aesthetics (Sculptra), and National Instructor, Allergan Facial Aesthetics.

References

1. Taylor SC. Overview of Skin of Color: Structure and Function. AAD 66th Annual Meeting, February, 2008.
2. Halder RM, Brooks HL, et al. Acne in ethnic skin. *Dermatol Clin*. 2003;21(4):609-615.
3. Grimes P. *Aesthetics and Cosmetic Surgery for Darker Skin Types*. Philadelphia: Lippincott Williams & Wilkins, 2008:15-26.
4. Berardesca E, Maibach. Ethnic skin: Overview of structure and function. *J Am Acad Dermatol*. 2003;48 (6s):S139-142.
5. Grimes P, Edison BL, et al. Evaluation of inherent differences between African American and white skin surface properties using subjective and objective measures. *Cutis*. 2004;73(6):392-396.
6. Nielloud F. Current Galenic Research Challenges in Human Dermatology: Application for the Development of Products for Sensitive and Atopic Skin. VIRBAC European Symposium Skin Biology and Innovations in Dermatology, March, 2003.
7. An S, Lee E, et al. Comparison and correlation between stinging responses to lactic acid and bio-engineering parameters. *Contact Dermatit*. 2007;57(3):158-162.
8. Basset A, Liautaud B, et al. *Dermatology of Black Skin*. Oxford: Oxford University Press, 1946.
9. Rawlins AV. Ethnic Skin Types: Are there Differences in Skin Structure and Function? *Int J Cosmet Sci*. 2006;28(2):79-93.
10. Pochi P, Strauss JS. Sebaceous Gland Activity in Black Skin. *Dermatol Clin*. 1988;6(3):349-351.
11. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease. *J Am Acad Dermatol*. 2002;46(2):S41-62.
12. Gfesser M, Worret WI. Seasonal Variations in the Severity of Acne Vulgaris. *Int J Dermatol*. 1996;35(2):116-117.
13. Bologna JL, Jorizzo JL, et al. *Dermatology*. Volume One, Second Edition. Philadelphia: Elsevier Science, 2008: 901-911.
14. Johnson BL, Moy HL, et al. *Ethnic Skin: Medical and Surgical*. St. Louis: Mosby, Inc., 1998.
15. Callender VD. Considerations for treating acne in ethnic skin. *Cutis* 2005;76(2 suppl):19-23.
16. Taylor SC. Cosmetic problems in skin of color skin. *Skin Pharmacol Appl Skin Physiol*. 1999;12(3):139-143.
17. Yeung CK, Ying Teo LH. A community-based epidemiological study of acne vulgaris in hong kong adolescents. *Acta Derm Venereol*. 2002;82(2):104-107.
18. Taylor SC, Cook-Bolden F. Acne vulgaris in skin of color. *J Am Acad Dermatol*. 2002;46:S98-106.
19. Cestari T. Cosmeceutical and Pharmaceutical Agents for Darker Skin Types. AAD 66th Annual Meeting, February, 2008.
20. Rubin MG. *Manual of Chemical Peels Superficial and Medium Depth*. Philadelphia: Lippincott Williams & Wilkins, 1995:44-50.
21. Grimes P. *Aesthetics and Cosmetic Surgery for Darker Skin Types*. Philadelphia: Lippincott Williams & Wilkins, 2008:73-77.
22. Fitton A, Goa KL. Azelaic Acid. A review of its pharmacological properties and therapeutic efficacy in acne and hyperpigmentary disorders. *Drugs* 1991;41(5):780-798.
23. Cunliffe WJ, Holland KT. Clinical and laboratory studies on treatment with 20% azelaic acid cream for acne. *Acta Derm Venereol*. 1989;143:31-34.
24. Gollnick H, Schramm M. Topical drug treatment in acne. *Dermatology*. 1998;196:119-125.
25. Thiboutot D. New treatments and therapeutic strategies for acne. *Arch Fam Med*. 2000;9:179-187.
26. Gibson JR. Rationale for the development of new topical treatments for acne vulgaris. *Cutis*. 1996;57(1 suppl):13-19.
27. Draelos ZD. *Procedures in Dermatology: Cosmeceuticals*. Philadelphia: Elsevier Saunders, 2005:103-109.
28. Badreshia-Bansal S, Draelos ZD. Insight into skin lightening cosmeceuticals for women of color. *J Drugs Dermatol*. 2007;6(1):32-39.
29. Aytemir MD, Hider RC. Synthesis of new antimicrobial agents; amide derivatives of pyranones and pyridinones. *Turkish J Chem*. 2003;27:445-452.
30. Draelos ZD. *Cosmetic Formulation of Products: Skin Care Skin Lightening Agents*. New York: Taylor and Francis Group LLC, 2006: 205-218.
31. Orth DS, Kabara JJ. *Cosmetic and Drug Microbiology*. New York: Informa Healthcare, 2005:163-184.
32. Usuki A, Ohashi A, et al. The inhibitory effect of glycolic acid and lactic acid on melanin synthesis in melanoma cells. *Exp Dermatol*. 2003;12 (2 suppl):43-50.
33. Helms RA, Quan DJ, et al. Textbook of Therapeutics: Drug and Disease Management Eighth Edition. Philadelphia: Lippincott Williams & Wilkins, 2006:203-256.
34. Leyden JJ, Rawlings AV. *Skin Moisturization*. New York: Marcel Dekker, Inc., 2002:323-352.
35. Baumann L. Cosmeceutical Critique: Licorice, Part 1. *Skin & Allergy News* 2007; 3:24.
36. Won S, Kim S, et al. Licochalcone A: A lipase inhibitor from the roots of glycyrrhiza uralensis. *Food Res. Intern*. 2007;40(8):1046-1050.
37. Baumann L, Rodriguez D, et al. Natural considerations for skin of color. *Cutis*. 2006;78: 2-19.
38. Rolewski SL. Clinical Review: Topical retinoids. *Dermatol Nurs*. 2003;15:447-465.
39. Draelos ZD. Retinoids in *Cosmetics Cosmeceutical Dermatology* 2005;18(1 suppl):3-5.
40. Lotti T, Theirs, BH, et al. *Dermatologic Clinics: Pigmentary Disorders*. Philadelphia: Elsevier Saunders, 2007:357-358.
41. Rendon MI, Gaviria JI. Review of skin-lightening agents. *Dermatol Surg*. 2005;31(7):886-889.
42. Kang S, Duell EA, et al. Application of retinol to human skin in vivo induces epidermal hyperplasia and cellular retinoid binding proteins characteristic of retinoic acid but without measurable retinoic acid levels or irritation. *J Invest Dermatol*. 1995;105:549-556.
43. Kang S. Mechanism of action of retinol. *Cosmetic Dermatology*. 2005;18(1 suppl):6-8.
44. Del Rosso JQ. The many roles of topical salicylic Acid. *Skin & Aging*. 2005;12(4):38-42.
45. Longshore SJ, Hollandsworth K. Acne vulgaris: One treatment does not fit all. *Cleve Clin J Med*. 2003;70:670-680.
46. Leyden JJ. A Review of the Use of Combination Therapies for the Treatment of Acne Vulgaris. *Journal of the American Academy of Dermatology* 2003;49(3 suppl):200-210.
47. Roberts WE. Chemical peeling in ethnic/darker skin. *Dermatol Ther*. 2004;17:196-205.
48. Brody HJ, Monheit GD. A history of chemical peeling. *Dermatol Surg*. 2000;26(5):405-409.
49. Effendy I, Kwangskuth C. Functional changes in human stratum corneum induced by topical glycolic acid: comparison with all-trans retinoic acid. *Acta Derm Venereol*. 1995;75(6):455-458.
50. Brody HJ. *Chemical Peeling and Resurfacing*. Second Edition. St. Louis: Mosby-Year Book, Inc., 1992:73-108.
51. Collins PS. Trichloroacetic Acid Peels Revisited. *J Dermatol Surg Oncol*. 1989;15(9):933-940.
52. Rubin MG. *Manual of Chemical Peels Superficial and Medium Depth*. Philadelphia: Lippincott Williams & Wilkins, 1995:130-153.
53. Baumann L. Cosmeceutical critique: salicylic acid. *Skin & Allergy News*. 2001;32(9):33.
54. Guttman C. Choice of peeling agent depends on patient characteristics. *Cosmetic Surgery Times*. 2003;6(2):18.
55. Lee HS, Kim IH. Salicylic Acid Peels for the Treatment of Acne Vulgaris in Asian Patients. *Dermatol Surg*. 2003;29(12):1196-1199.