Treatment Strategies for Pigmentation Disorders in Skin of Color

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Dyschromia can be especially disfiguring in patients with skin of color. Exogenous ochronosis, postinflammatory hyperpigmentation (PIH), and vitiligo often are highly noticeable in darker skin types and cause anguish for individuals affected by these conditions. This article will review the literature regarding current medical and procedural therapies for pigmentary disorders to update physicians on specific treatment options that are available for patients with darker skin types. Although treatment of these disorders remains difficult, there is an increasing number of therapeutic options that could lead to improvement in both the cosmetic appearance of the skin and the quality of life of patients who are affected by these psychologically distressing conditions. Most of the existing literature on the safety and efficacy of these treatments consists of case reports and cohort studies; there is a lack of larger randomized controlled trials. Further studies are necessary to yield safe reproducible results for treating pigmentary disorders in patients with skin of color. *Cosmet Dermatol.* 2011;24:524-531.

t first glance, the effects of cutaneous pigmentation disorders may seem purely cosmetic in nature, but they also can result in a profound psychological burden for patients, especially when located on the face, neck, or hands. Although pigmentation disorders can affect all skin types, individuals with darker skin, including Asians, blacks, Latinos, and American Indians, are more susceptible. Ethnic minorities account for more than 30% of the US population, a percentage that is projected to increase to approximately 50% by 2050¹; therefore, familiarity with the skin disorders that commonly affect patients with darker skin and the available treatment options is crucial to the practicing dermatologist. This review will provide updates on current management options for 3 pigmentation disorders: exogenous ochronosis, postinflammatory hyperpigmentation (PIH), and vitiligo.

EXOGENOUS OCHRONOSIS

Exogenous ochronosis is a cosmetically disfiguring hyperpigmentation disorder that is highly prevalent in blacks

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and rarely affects white individuals. Hardwick et al² found that 15% of black males and 42% of black females attending general outpatient departments in 2 South African hospitals presented with ochronosis. Sixty-nine percent of the patients with ochronosis also reported prior use of topical skin lighteners.² Exogenous ochronosis also has been commonly reported in Asians who use hydroquinone (HQ) to treat melasma.³

Clinically, ochronosis presents as a bluish gray, asymptomatic, hyperpigmented discoloration that typically affects the malar eminences, temples, inferior cheeks, neck, back, and extensor surfaces of the extremities. Coarseness, erythema, and some pigmentation of the skin can be present in some mild cases. Disease progression often is marked by hyperpigmentation with darkly pigmented, coalescing papules and associated atrophy. Chronic and severe cases may result in the development of papulonodules. Yellow-brown or green globules and ochronotic fibers are observed in the papillary dermis on dermatopathologic evaluation. Chronic cases demonstrate ochronotic colloid milium, representing the degeneration of the ochronotic fibers and granulomas.

Exogenous factors that have been implicated in the development of ochronosis include topical use of HQ, which is the most commonly reported cause; topical use of phenol for leg ulcers; skin-lightening soaps and creams that contain mercuric compounds; resorcinol found in some over-the-counter topical acne treatments; and injectable quinine and other oral antimalarials.

Management of Ochronosis

Topical—Treatment of ochronosis remains difficult. The first step in any treatment plan should be avoidance of the offending agent; however, an extended period of time without contact with the agent is needed to yield noticeable improvement.⁴ Sun avoidance and sunscreens also have shown modest efficacy.⁵ Variable results have

been reported in the use of retinoic acid with some patients developing undesired transient hyperpigmentation, which underscores the sensitivity of darker skin types to irritation. Tetracycline has been shown to promote clearance of papular sarcoidlike ochronosis; however, this result has only been reported in 1 patient.⁶ Overall, ochronosis remains largely refractory to topical treatment.

Procedural-Early procedural approaches such as chemical peels with trichloroacetic acid and cryotherapy with liquid nitrogen were reported in 1 black patient with no significant improvement of ochronosis.4 The efficacy and safety of these treatments as monotherapies have not been reported. Advances in laser technology have increased the success rate in managing dyschromia associated with ochronosis. As reported by Bellew and Alster,7 laser therapy is believed to disrupt the dermal ochronotic pigment fibers, leading to their subsequent phagocytosis and removal through lymphatic drainage or transepidermal elimination. In this study, 2 patients with exogenous ochronosis were treated bimonthly with a Q-switched alexandrite laser at a fluence of 7 to 8 J/cm² using nonoverlapping 3-mm collimated spots; the patients also were instructed to avoid sun exposure. Progressive fading of hyperpigmentation was noted, and histologic evaluation after 6 treatments revealed a lack of dermal pigment deposits.7

Other pigment-specific lasers are thought to evoke a similar mechanism of pigment clearance, including the Q-switched 694-nm ruby and Q-switched 1064-nm Nd:YAG lasers. The Q-switched 1064-nm Nd:YAG laser has been successfully used for the treatment of dyschromia (Figure 1). In another study, a patient who was treated with a Q-switched ruby laser at 7 J/cm² for discoloration secondary to decades of HQ cream 2% use showed improvement⁸; however, physicians must be cautious, as the Q-switched 694-nm ruby laser has a shorter



Figure 1. A black female with exogenous ochronosis on the left side of the forehead and temporal regions secondary to chronic use of hydroquinone before (A) and after treatment with the Q-switched 1064-nm Nd:YAG laser (B).

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wavelength, resulting in greater absorption at the melanocyte level. This possibility of decreased penetration into the dermis may not be desirable for the treatment of ochronosis given that it primarily occurs in patients with skin of color, limiting utility of the laser in this setting.

One case report of a black female patient who was treated with a combination of dermabrasion and a CO_2 laser achieved skin lightening with the CO_2 laser used in areas that were not amenable to dermabrasion, such as around the eyes, nose, and forehead.⁴

It should be noted that topical and nonpharmaceutical therapies should be used in combination with procedural methods because they are not likely to demonstrate high efficacy when used as monotherapy. A summary of therapeutic approaches for the treatment of exogenous ochronosis are highlighted in Table 1, and Figure 2 provides a treatment algorithm for exogenous ochronosis.

POSTINFLAMMATORY HYPERPIGMENTATION

Postinflammatory hyperpigmentation in the epidermis presents as a tan or brown discoloration, while PIH in the dermis has a blue-gray appearance. Without treatment, dyschromia can take months to years to resolve and may be permanent. Postinflammatory hyperpigmentation is most commonly observed in Fitzpatrick skin types III to VI, which includes the majority of patients with skin of color. The development of PIH following acne likely is the most common cause of PIH seen by dermatologists. One study (239 blacks, 55 Hispanics, 19 Asians) showed that 65.3% of blacks, 52.7% of Hispanics, and 47.4% of Asians developed acne-induced PIH.¹⁰

Management of PIH

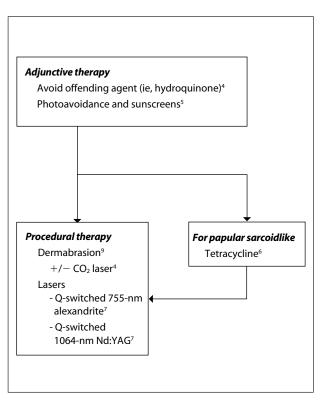
Nonpharmaceutical—Treatment of PIH should begin with management of the cause of inflammation. For instance, if the patient's PIH is secondary to acne, optimal acne treatment should be administered to reduce the patient's frustration with the occurrence of dyschromia. The same should be done with other inflammatory processes. Patients also should be counseled on the development of PIH given that they may erroneously continue treating areas with previously prescribed medications for the inflammatory condition. Patients often resort to tanning in an attempt to even out the pigmentation; however, use of photoprotection with sunscreen and photoavoid-ance should be part of patient counseling, as pigmentary lesions tend to darken with tanning.

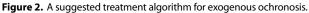
Topical—The most commonly used topical agent for depigmentation is HQ. Hydroquinone works by inhibiting the enzyme tyrosinase, which blocks the conversion of dihydroxyphenylalanine to melanin. However,

TABLE 1

Therapeutic Approaches for the Treatment of Exogenous Ochronosis

Nonpharmaceutical	Topical	Procedural
Discontinuation of offending agent ⁴	Sunscreens⁵	Dermabrasion ⁹
Sun avoidance⁵	Tetracycline ⁶	Dermabrasion plus CO₂ laser⁴
	Retinoic	. 2
	acid ⁹	Q-switched 694-nm
		ruby laser ⁸
		Q-switched 755-nm
		alexandrite
		laser ⁷
		Q-switched
		1064-nm Nd:YAG laser ⁷





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monotherapy has not been as successful as the use of a combination of topical products. Patients in an open-label study who were treated twice daily with microencapsulated HQ 4% and retinol 0.15% with antioxidants for 12 weeks demonstrated improvement in their dyschromia. The investigators observed reductions in lesion size and darkness as early as 4 weeks into treatment, while 63% (12/19) of participants had either 75% overall improvement or complete clearing of hyperpigmented lesions after 12 weeks.¹¹ In addition to causing exogenous ochronosis, which was previously discussed, the side effects of HQ include contact dermatitis, nail discoloration, permanent leukoderma, and halo effect.12 Retinoids,13 tazorotene,14 adapalene,15 azelaic acid,16 and N-acetylglucosamine or N-acetylglucosamine/niacinamide combination¹⁷ also have been shown to improve PIH.

Procedural—Superficial chemical peels have been shown to be effective in the treatment of PIH, even in patients with darker skin.¹⁸ Frequently used agents include glycolic acid (20%–70%) and salicylic acid (20%–30%).^{18,19} A study of 10 patients with Fitzpatrick skin types IV to VI showed that salicylic acid peels were safe when used in this population; although patients rated the peels as clinically effective, blinded raters found peels to be less effective.¹⁹

Photodynamic therapy, lasers, and fractional photothermolysis are now increasingly used for the treatment of PIH. Three cases of PIH in Asian patients treated with a low-fluence 1064-nm Q-switched Nd:YAG laser showed maintenance of improvement at 2 months after final treatment. Patients underwent 5 treatment sessions that were delivered weekly to the entire face, with settings of 1.9 to 2.6 J/cm², a 6-mm spot size, and 3 passes with appropriate overlapping.²⁰ Figure 3 shows PIH secondary to folliculitis that was treated with the Q-switched 1064-nm Nd:YAG laser. A study using fractional photothermolysis demonstrated improvement of dyschromia after 5 sessions administered 1 to 2 weeks apart using the 1550-nm wavelength Fraxel SR750 laser (Reliant Technologies, Inc) at a pulse energy of 6 to 10 mJ and a final density of 2000 to 3000 microscopic thermal zones/cm². After 2 months, 50% to 75% improvement in dyschromia from baseline was observed in 1 patient and was maintained 3 months after cessation of treatment.²¹ Six PIH patients treated with a 1550-nm nonablative fractional laser demonstrated no significant improvement in all outcome measures, including reflectance spectroscopy, melanin index, number of melanocytes, and amount of dermal melanin between treated and control skin.²²

Blue light photodynamic therapy with aminolevulinic acid 20% has been used in combination with daily HQ cream 4% for 4 months in a black patient with both acne and associated PIH.²³ Visible improvement was

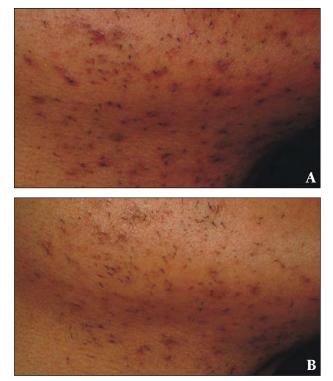
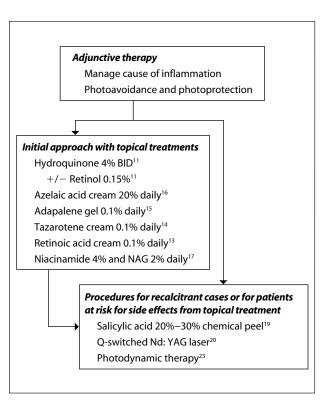
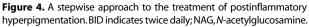


Figure 3. Brown-pigmented perifollicular macules in the mandibular area of a male patient secondary to folliculitis before (A) and after treatment with the Q-switched 1064-nm Nd:YAG laser (B).





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observed after only 2 monthly photodynamic therapy sessions, and continued resolution of dyschromia persisted after 4 months. Of note, concurrent acne treatments included topical clindamycin/benzoyl peroxide and tazarotene throughout the study.²³ A stepwise approach to PIH is suggested in Figure 4.

VITILIGO

Vitiligo results in milky white, cosmetically disfiguring patches that are especially noticeable in patients with skin of color because of the contrast observed in darker skin types. Vitiligo is a progressive disorder that is characterized by the destruction of melanocytes and affects up to 2% of the worldwide population. Commonly affected areas include the face, neck, scalp, ventral wrists, dorsal hands, and genitals, as well as mucous membranes. Proposed etiologies for the disease include autoimmune, cytotoxic, melanocyte defect, oxidant-antioxidant, and neural mechanisms.²⁴

Management of Vitiligo

Nonpharmaceutical—Nonpharmacologic approaches have included cosmetic camouflage products, self-tanners, and cosmetic tattooing. One study showed that patients who used camouflage techniques had significantly improved emotional symptons (P=.024) compared to those who did not use camouflage.²⁵ Longer-lasting camouflage options include a color-matched simulated second skin that is sprayed on and can last up to 5 days (Microskin, Microskin & Simulated Skin Inc). This product has improved psychosocial functioning in pediatric burn patients.²⁶ Improvement in the appearance of lesions after cosmetic tattooing also has been demonstrated in localized stable vitiligo.²⁵

Topical—Topical steroids have been used for treatment of vitiligo for decades and remain the most commonly used therapies. Systemic corticosteroids also have been shown to improve vitiligo symptoms; however, the side effects caused by systemic steroids preclude their extensive use. A thorough discussion of the risks and benefits must accompany the use of systemic steroids for a potentially chronic disease. Side effects of topical steroids include skin atrophy, telangiectasia, striae, adrenal insufficiency, and infections, among others. The repigmentation effects of topical steroids may be increased when combined with topical calcipotriene; however, calcipotriene alone has been shown to be inferior to topical steroids.²⁷

Topical calcineurin inhibitors such as tacrolimus also can promote repigmentation of vitiligo lesions in children. Thirty patients evaluated as part of a prospective study found that tacrolimus ointment 0.1% applied twice daily resulted in some repigmentation in 83.3% (25/30) of patients after 4 months. Seventy-six percent to 100% repigmentation was noted in 37.1% of patients with head and/or neck involvement, and initial repigmentation typically was noted after 6 weeks of treatment.²⁸ Although tacrolimus may cause a burning sensation in the area of application, it is thought to be a better option for sensitive areas given that it does not promote skin atrophy.²⁹

Phototherapy—Phototherapy and photochemotherapy, to a more limited extent, have remained popular in the treatment of vitiligo given their effectiveness. The superiority of narrowband UVB (NB-UVB) to psoralen plus UVA has been reported. In one study, 64% (16/25) of patients in the NB-UVB group showed an improvement of more than 50% in body surface area affected compared to 36% (9/25) of patients in the psoralen plus UVA group.30 Narrowband UVB also has been utilized in conjunction with pseudocatalase. In their study utilizing this regimen in pediatric vitiligo patients, Schallreuter et al³¹ reported more than 75% repigmentation in 93% (66/71) of patients receiving treatment of the face and neck, 79% (48/61) of patients receiving treatment of the trunk, and 73% (40/55) of patients receiving treatment of the extremities. Phototherapy treatment options have been extensively covered in the literature.30-33

Lasers-High-energy monochromatic light can be precisely delivered to depigmented areas with the use of the excimer laser. Prior uses of this technology include treatment of postresurfacing leukoderma, mature hypopigmented striae, and psoriasis. A retrospective chart review of 97 chronic vitiligo patients who were treated with the 308-nm xenon chloride excimer laser demonstrated that 50.6% (112/221) of vitiligo patches treated showed 75% pigmentation or more, 25.5% (56/221) achieved 100% pigmentation, and 64.3% (142/221) showed 50% pigmentation or more.³⁴ As with other light delivery techniques, facial lesions showed a greater response to treatment than those in other areas.³¹ The excimer laser yielded a better repigmentation response at earlier stages of the disease than in more chronic lesions, and long-term use with high-cumulative UV light elicited better responses.35

A multicenter, randomized, investigator-blinded study comparing 308-nm monochromatic excimer light and NB-UVB demonstrated that 37.5% (6/16) of the lesions treated with the monochromatic excimer light achieved 76% to 100% repigmentation versus 6% (1/16) treated with NB-UVB after 6 months of twice-weekly treatment.³⁶ In contrast, a recent randomized comparison of excimer laser versus NB-UVB phototherapy after punch grafting showed no significant difference in repigmentation between the 2 groups after 3 months of therapy. Importantly, excimer laser treatment had a 71.4% lower

cumulative UV dose than NB-UVB.³⁷ When selecting a treatment modality, not only repigmentation scores but also the possible side effects from cumulative UV dose should be evaluated. Thus patients with substantial sun damage or others at risk can benefit from the more precise delivery and lower cumulative dose of UV light with the excimer laser.

Surgical—The goal of surgical approaches is to restore melanocytes in areas affected by vitiligo. These approaches include suction blister grafting, split-thickness grafting, punch grafting, follicular grafting, and cultured and noncultured melanocyte transplantation.³⁸ Invasive procedures may be limited in patients susceptible to koebnerization, which can lead to scarring, graft failure, and infection. Njoo et al³⁹ reported in a systematic review of 63 studies that suction blister grafting and split-thickness grafting demonstrated the highest success rates, while punch grafting showed the highest rate of adverse effects, including a cobblestonelike appearance and scar formation at the donor site.

With the suction blister grafting technique, blisters are created at epidermal donor sites and are then grafted to prepared areas of vitiligo-affected skin.⁴⁰ The advantages of this technique include a lack of depigmentation and scarring in donor areas. In split-thickness grafting, the donor site is obtained by using a hand dermatome or a shaving blade. Although split-thickness grafting has the highest success rates, limitations include difficulty obtaining uniform-thickness grafts, resultant stuck-on effects, persistent hyperpigmentation, and scars on donor areas.⁴¹ A summary of therapeutic approaches for the treatment of vitiligo are highlighted in Table 2, and a treatment algorithm is provided in Figure 5.

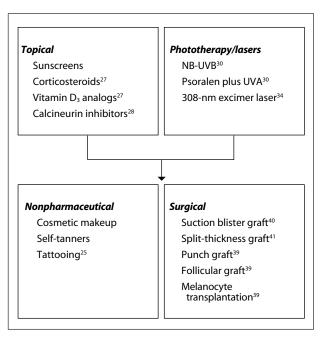


Figure 5. A stepwise approach to the treatment of vitiligo. NB-UVB indicates narrowband UVB.

Therapeutic Approaches for the Treatment of Villigo			
Nonpharmaceutical	Topical	Phototherapy/Lasers	Surgical
Cosmetic makeup	Sunscreens	NB-UVB ³⁰	Suction blister graft ⁴⁰
Self-tanners	Corticosteroids ²⁷	Psoralen plus UVA ³⁰	
Tattooing ²⁵	Vitamin D ₃ analogs ²⁷	308-nm excimer laser ³⁴	Split-thickness graft ⁴¹
	Calcineurin inhibitors ²⁸		Punch graft ³⁹
			Follicular graft ³⁹
			Melanocyte
			transplantation ³⁹
Abbreviation: NB-UVB, narrowband UVB.			

Therapeutic Approaches for the Treatment of Vitiligo

Table 2

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CONCLUSION

The number of patients with darker skin types who seek treatment of dyschromia will increase as the population with skin of color in the United States continues to grow; therefore, it is essential for the practicing dermatologist to be familiar with the presentation and management of pigmentation disorders in patients with skin of color. Discontinuing offending agents, managing exacerbating conditions, and preventing complications form the foundation for most treatment protocols. Topical agents in conjunction with or followed by procedural approaches such as light therapy and lasers also can be employed and have shown promising results in treating skin discoloration.

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