Beyond Conventional Paradigms: Rethinking the Evaluation and Management of Melasma

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Melasma is a chronic hyperpigmentation disorder with a high recurrence rate. Advances in pathogenesis, diagnosis, and treatment have shifted dermatologic approaches for both initial management and long-term care. These advances highlight the need to move beyond conventional paradigms for melasma to adopt a more comprehensive and holistic approach to evaluation and management.

Diagnosis: Beyond the Wood Lamp

Diagnosis of melasma is primarily clinical, based on visual examination, with tools such as a Wood lamp (320-400 nm) aiding in classification as epidermal, dermal, or mixed types.[1] Dermoscopy is another useful tool that commonly demonstrates a brown reticular pseudonetwork, vascular patterns, and brown clods.[2] Reflectance confocal microscopy allows detailed assessment of pigment distribution across skin layers and may serve as a useful diagnostic adjunct.[3] Two-photon excitation microscopy also has shown concordance with reflectance confocal microscopy in identifying key pathologic features of melasma and allows quantitative assessment of pigment burden.[4,5] Biopsy remains warranted in cases when the diagnosis is unclear.[6,7] These advanced tools provide additional options for noninvasive imaging of melasma, which may be useful during both diagnosis and treatment.

Pathogenesis: Beyond the Melanocyte

Recent insights into pathogenesis have shifted the view of melasma from a purely melanocyte-driven disorder to one involving complex epidermal-dermal interactions influenced by chronic UV and visible light exposure and sustained cutaneous inflammation. Evidence suggests involvement of additional cell types and structural components, including epidermal barrier dysfunction, basement membrane alterations, senescent fibroblasts, mast cell activity, vascular remodeling, and dermal solar elastosis. Senescent fibroblasts secrete melanogenic and angiogenic mediators (including stem cell factor, vascular endothelial growth factor, endothelin 1, and matrix metalloproteinases) while mast cell degranulation releases histamine, tryptase, and other proteases that drive melanocyte activation, extracellular matrix degradation, and persistent hyperpigmentation.[8] New research highlights the importance of epidermal-dermal communication in melasma disease activity.[8,9] Exposure to UV and visible light leads to keratinocyte injury and fibroblast dysfunction, promoting the release of inflammatory and melanogenic mediators that stimulate melanocytes and weaken the basement membrane.[8] Mast cell activation and vascular signaling also have been implicated, reinforcing the contribution of inflammation and dermal remodeling to ongoing pigmentation.[9] This broader understanding helps explain the difficulty of sustaining long-term remission.[8,9] The multifaceted and evolving understanding of melasma's complex pathogenesis highlights areas for future therapeutic targets beyond melanin, which may help lead to greater clearance and remission periods.

Treatment: Beyond Hydroquinone

Melasma treatment has shifted toward a longitudinal approach reflecting its chronic relapsing nature. Effective management should include combination therapy of broad-spectrum photoprotection, topical therapies, systemic therapies (when appropriate), and adjunctive procedural modalities, while emphasizing the importance of maintenance therapy and relapse prevention.[10,11] Growing evidence demonstrates that UV and visible light contribute to melanogenesis and prolonged pigmentation,

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particularly in individuals with skin of color.[12,13] Visible light, particularly within the high-energy blue wavelength spectrum (400-500 nm), induces reactive oxygen species and stimulates melanogenesis, resulting in persistent hyperpigmentation and exacerbation of melasma in darker skin types.[13] Iron oxide, a mineral-based physical filter commonly used in tinted mineral sunscreens, enhances protection from visible light, thus improving melasma outcomes.[12,13] In a randomized double-blind placebo-controlled trial, oral polypodium leucotomos extract, an antioxidant with photoprotective effects, improved Melasma Area and Severity Index (MASI)/modified MASI (mMASI) scores and melasma-rated quality of life measures when used as an adjunct to sunscreen with or without topical hydroquinone.[14]

Topical therapy serves as the mainstay of melasma treatment. Hydroquinone- and retinoid-based regimens including triple-combination therapy remain an effective gold standard for active disease; however, there still are concerns about irritant dermatitis with both as well as ochronosis with long-term use of hydroquinone.[15] Recent studies highlight the efficacy of nonhydroquinone topical therapies such as azelaic acid, tranexamic acid (TXA), thiamidol, cysteamine, metformin, malassezin, 2-mercaptonicotinoyl glycine, niacinamide, kojic acid, ascorbic acid, and botanical-derived compounds, many of which demonstrate reductions in disease severity and more favorable tolerability profiles.[16-19] Combinations of these ingredients can allow for addressing the various pathogenic factors of melasma beyond pigmentation, including vascularity, inflammation, and solar damage.

Systemic therapy, particularly oral TXA, has emerged as an option for patients with moderate to severe or refractory melasma. Clinical trials and observational studies demonstrate improvement with oral TXA; however, relapse after discontinuation is common, emphasizing the importance of careful patient selection, established treatment duration, and concurrent maintenance therapy.[16,20] Although it is well tolerated, adverse effects include gastrointestinal discomfort, menstrual irregularities, and headache. Additionally, prescreening for contraindications and clotting risk factors is needed to avoid thromboembolic events.[21]

Procedural interventions are best used as adjunctive therapies rather than primary treatment. Superficial and medium peels can be used depending on baseline skin type.[22] Platelet-rich plasma is a promising adjunctive therapy for melasma, demonstrating reductions in MASI scores following intradermal or microneedling-assisted delivery, likely mediated through growth factor–driven inhibition of melanogenesis and modulation of tyrosinase activity. Platelet-rich plasma promotes dermal remodeling through angiogenesis, collagen synthesis, and extracellular matrix production improving skin texture and pigmentation.[23] Botulinum toxin A may improve pigmentation by modulating melanogenesis as well as inflammatory and vascular pathways.[24]

Radiofrequency microneedling provides a dermal-targeting therapeutic approach, with some evidence showing that monthly treatments can help maintain improvements achieved with conventional therapy by modulating photoaged dermal structures impacted by melanogenic signaling.[25] Histopathologic correlation studies suggest that microneedling used alone or as a delivery platform alongside topical agents may be beneficial in dermal-predominant disease, while laser-based therapies should be reserved for recalcitrant cases due to the risk for postinflammatory hyperpigmentation and melasma recurrence, particularly in those with darker skin types.[26] Lasers such as Q-switched 1064-nm Nd:YAG as well as nonablative lasers used in conservative settings are options for melasma treatment, including in patients with skin of color.[26,27] Laser toning with serial low-fluence (<3 J/cm^2), large-spot 1064-nm Nd:YAG has been used to reduce inflammation and risk for postinflammatory hyperpigmentation.[28] Additionally, randomized split-face data demonstrate that picosecond 1064-nm devices achieve comparable reductions in mMASI scores to traditional nanosecond devices, and combination strategies incorporating intense pulsed light (IPL) have shown greater MASI improvement compared with IPL alone.[28,29] However, IPL generally is limited to lighter skin phototypes due to the risk for postinflammatory hyperpigmentation in darker skin.[30]

Lastly, long-term management requires patient education on the importance of year-round maintenance therapy, consistency, and compliance. Reinforcing adherence to photoprotection, supporting barrier repair, and setting expectations regarding prognosis are essential components to optimizing melasma treatment outcomes.[12]

Future Insights: Beyond the Current State of Melasma Research and Treatment

Future advances in melasma management likely will focus on improving disease assessment and long-term treatment durability. Tools such as the MASI and mMASI are widely used but are limited by interobserver variability and reduced sensitivity in darker skin types, highlighting the need to incorporate objective measures such as colorimetry.[10,26] There also is a need for studies that relate clinical improvement to underlying pathology. Histopathologic correlation remains limited across most therapeutic trials, and more studies should assess long-term outcomes and quality-of-life measures given the relapsing nature of melasma.[26]

Future interventions will continue to move past the treatment of pigment alone. Increasing recognition of vascular, inflammatory, and barrier-related contributions to melasma, as well as targeting of other cell types affected by melasma, will be important considerations in future treatment innovations.[8,11] In summary, improved inclusion of patients with skin of color in clinical trials, expansion of clinical outcomes measures and objective

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parameters of disease evaluation, novel approaches to treatment and relapse prevention, and greater attention to patient adherence and education will be essential to achieving advancements in melasma care.[12]

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