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Managing Hyperpigmentation Across the Spectrum of Skin Tones

Featuring:



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Andrew Alexis, MD, MPH, Professor of Clinical Dermatology and Vice-Chair for Diversity and Inclusion at Weill Cornell Medicine in New York, NY, and Hilary Baldwin, MD, Medical Director of the Acne Treatment & Research Center in Morristown, NJ, recently hosted a webinar on the role that Melasyl, the novel molecule that powers La Roche-Posay's Mela B Serum, plays in fading hyperpigmentation across skin tones.

Hyperpigmentation remains one of the most vexing skin conditions, and people with darker skin types are often harder hit by dark spots than their counterparts with lighter complexions. The gold standard for addressing hyperpigmentation has long been hydroquinone, but use of this cream is associated with skin rashes, facial swelling, and ochronosis.

This is why dermatologists are so excited about the latest innovation in treating hyperpigmentation: La Roche-Posay's Mela B3 Dark Spot Serum & Mela B3 UV Daily Moisturizer SPF 30. Powered by Melasyl, this new multi-patented pigment-correcting product line reduces post-acne marks, sunspots, age spots, and even persistent dark spots across skin tones.

Hyperpigmentation is one of the leading reasons that patients with darker skin tones visit a dermatologist, according to data from the National Ambulatory Medical Care Survey.[1] Similarly,



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Ask the Expert

Q:

How soon should acne scarring be treated?

A:

"The earlier, the better."
-Dr. Alexis

a community-based survey out of Henry Ford Hospital in Detroit, MI, identified uneven skin tone and skin discoloration as the top skin concerns facing people of Middle Eastern ancestry.[2] Another survey found that uneven skin spots and dark spots were among the top five dermatologic conditions seen among patients of South Asian descent.[3]

Hyperpigmentation can occur as a primary dermatological condition, such as melasma, or secondary to another dermatological condition such as acne or after a procedure. Post-inflammatory hyperpigmentation (PIH) is the most common hyperpigmentation disorder that dermatologists see in practice.

"[Patients] come in with dark spots, with red spots that often bother them more than the acne lesions themselves, so it's something that we have to deal with on a daily basis," says Dr. Baldwin. "If I don't address the hyperpigmentation at the same time that I'm addressing the acne, the patient is usually not satisfied with my care." Dr. Baldwin does take care of the active lesions first, but also focuses on the discoloration.

It's important to determine the underlying cause of PIH and address it to keep it from coming back in the future. Certain patient behaviors may also cause PIH, including the use of harsh skin care products or overuse of a topical retinoid. PIH can also occur after aesthetic procedures.

Other medical pathways that lead to PIH include allergic hypersensitivity, infectious disorders, and autoimmune disorders.[4]

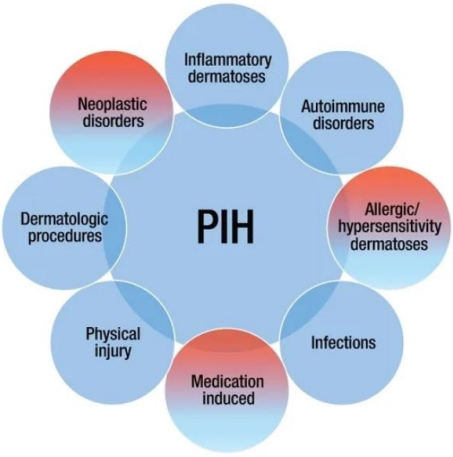
"You certainly wouldn't want to just focus on the PIH and not manage the underlying process that led to it. Otherwise, the patient will continually get new areas of PIH," says Dr. Alexis.

Understanding How Hyperpigmentation Affects Quality of Life

Hyperpigmentation places a huge burden on many patient populations.

Fully 50% of respondents are concerned about pigmentary disorders, according to an extensive international study looking at how these disorders affect quality of life conducted by La Roche-Posay and IPSOS.

PIH — A Sequela of a Broad Range of Dermatoses



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USA: National Ambulatory Medical Care Survey (1993-2009)

AFRICAN AMERICAN	ASIAN/PACIFIC ISLANDER	HISPANIC/LATINO
1. Acne	1. Acne	1. Acne
2. Dermatitis, unspecified	2. Dermatitis, unspecified	2. Dermatitis, unspecified
3. Seborrheic dermatitis	3. Benign neoplasm	3. Psoriasis
4. Atopic dermatitis	4. Psoriasis	4. Benign neoplasm
5. Dyschromia	5. Seborrheic keratosis	5. Viral warts
6. Psoriasis	6. Atopic dermatitis	6. Actinic keratosis
7. Alopecia	7. Viral warts	7. Seborrheic keratosis
8. Keloid scar	8. Urticaria	8. Sebaceous cysts
9. Viral warts	9. Sebaceous cysts	9. Rosacea
10. Sebaceous cysts	10. Seborrheic dermatitis	10. Dyschromia

The most common pigmentary disorder was solar lentigo (27%), followed by axillary hyperpigmentation (18%), periorbital hyperpigmentation (15%), PIH (15%), melasma (11%), and vitiligo (8%), the survey showed. There was a higher prevalence of pigmentary disorders among women and older people. Individuals older than 50 cited solar lentigo as a pigmentary disorder of concern, while respondents younger than 30 cited PIH and vitiligo as their main pigmentary disorders of concern.[5]

To capture the degree of stigmatization that affects patients with pigmentary disorders, researchers used the Patient Unique Stigmatization Holistic tool in Dermatology (PUSH-D).[6] The instrument measures stigma on an ascending scale from zero to 68, with zero denoting no stigma and 68 denoting a high stigma. PUSH-D is easily understood, validated, and available in more than 20 languages.

Among individuals who reported having melasma or PIH, more than half felt it necessary to conceal or hide the visible parts of their affected skin, and more than one-third of people with melasma and PIH refused contact with the public as a result of their dark spots.

When asked 'have you ever felt less loved by your family or friends?' approximately a quarter of folks with melasma and PIH said that they have at least sometimes felt less loved by their family or friends as a result of their pigmentary disorder.

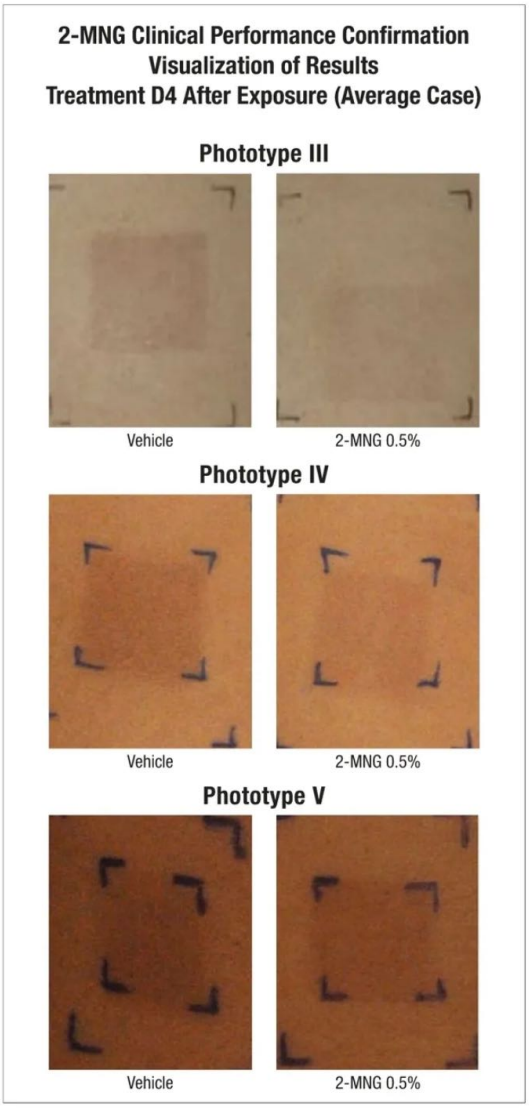
Similarly, when asked if they faced discrimination at work, roughly a quarter of people with melasma and PIH said yes.

"These are really staggering numbers," Dr. Alexis says. "The impact on our patients is really tremendous for all of the forms of post-inflammatory changes," agrees Dr. Baldwin. "I am not surprised that they feel that they face discrimination at work [but] the thing that moves my heart is feeling less loved by their family and friends." It may be that they feel so bad

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about themselves that they assume that people love them less, she speculates.

"These disorders have a tremendous impact on quality of life, including stigmatization, and there's no question that when patients present to us with concerns about hyperpigmentation, we do all we can to manage the condition," Dr. Baldwin says.

There are numerous strategies to prevent or curb hyperpigmentation. One approach is to inhibit the production of melanin by limiting the enzyme tyrosinase. Another calls for disrupting the transfer of melanosomes from the melanocyte to the keratinocyte. A third strategy involves removing excess epidermal melanin, and a fourth calls for the removal of dermal pigment.[7]

None of these strategies will be effective without the regular application of sunscreen. "Photo protection is clearly a foundational step when we're managing hyperpigmentation together with these other strategies that we leverage," says Dr. Alexis.

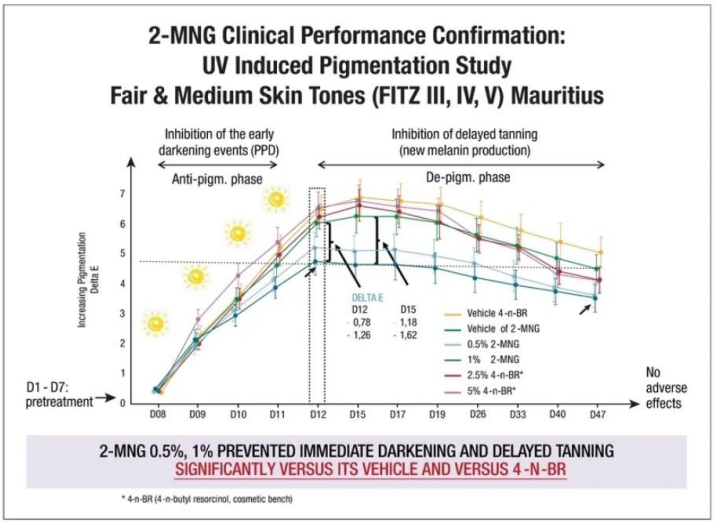
The gold standard for treating hyperpigmentation is hydroquinone, but this treatment is not without its downsides, which include a "halo" of hypopigmentation on perilesional skin, irritant contact dermatitis, and exogenous ochronosis.[8]

Drs. Baldwin and Alexis commonly see the "halo" of hypopigmentation in their practices, particularly when patients use hydroquinone as a spot treatment for the hyperpigmented macules that accompany acne.

"Often, the patients don't even see [the halo] themselves until you point it out," says Dr. Baldwin, noting the macules can be extremely small. "[It is] impossible to put the hydroquinone just on [the macule] without getting the surrounding skin."

Clinicians have long sought alternative treatment because of the adverse events that can occur with use of hydroquinone. Some of those alternatives are available by prescription, and some are available over the counter. In the prescription space, hydroquinone alternatives such as topical retinoids, topical azelaic acid, and oral tranexamic acid are available. In the

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non-prescription space, cosmeceuticals like soy, licorice extract, arbutin, niacinamide, vitamin C, lignin peroxidase, and kojic acid are considered hydroquinone alternatives.[9,10]

Exploring the Science Behind Mela B3

New to the hyperpigmentation scene and born from 18 years of research is 2-mercaptonicotinoyl glycine (2-MNG) or Melasyl (Mela B3, La Roche-Posay). Mela B3 possesses unique modes of action with respect to inhibiting melanin synthesis and ultraviolet-induced (UV-induced) pigmentation, notes Dr. Alexis.[11] This launch marks a breakthrough in pigmentation science.

The molecule 2-MNG captures various melanin intermediates, including DOPA and DOPAquinone. Other melanin intermediates such as DHICAquinone and DHIquinone are involved in eumelanin synthesis, while cysteine and Cysteinyldopa are involved in pheomelanin synthesis. Introducing 2-MNG into the process of melanin synthesis leads to the formation of adducts, which are removed from the process of melanin synthesis, so that melanin precursors are essentially quenched with 2-MNG.[12]

"[2-MNG] is a novel molecule that also works by a novel mechanism," says Dr. Alexis. "It's not simply a tyrosinase inhibitor. It actually works by tackling precursors of melanin synthesis. What Melasyl does…is bind to these melanin precursors and ultimately reduce the production of both eumelanin and pheomelanin in this way."

The molecule has demonstrated safety and efficacy through in vitro and in vivo models. A network meta-analysis compared the efficacy of Melasyl to that of other skin lightening therapies such as hydroquinone, kojic acid, niacinamide, tranexamic acid, arbutine, and several others and concluded that Melasyl demonstrated the strongest efficacy.[13,14]

Dr. Alexis highlighted research on the use of 2-MNG on skin phototypes III, IV, and V that was exposed to sun or UV. The studies demonstrated that 2-MNG was effective in the immediate phase of darkening during UV exposure and the delayed phase of new melanin production. The delayed phase is measured by an additional increase in pigmentation up to seven days after the last UV exposure.[14]

Ask the Expert

Q:

Do you use Mela B3 by itself or combine it with other products?

A:

"I am not aware that it has been tested with other products other than in the context of studies. In real-world practice, when treating a whole range of different skin types and severities of hyperpigmentation, I'll often combine Mela B3 with a prescription product."

-Dr. Alexis

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"The bottom line is that 2-MNG was shown to inhibit both immediate pigment darkening and delayed darkening," says Dr. Alexis.

"The bottom line is that 2-MNG was shown to inhibit both immediate pigment darkening and delayed darkening," says Dr. Alexis.

The reduction in hyperpigmentation is very impressive, adds Dr. Baldwin.

There are several ways to target dark spots. They include:

- Decreasing the melanin precursors
- Inhibiting melanogenesis or melanin transfer
- Exfoliation to remove the keratinocytes, which have extra pigment
- Increasing cell renewal to eliminate the excess melanin
- Reducing inflammation
- Improving the barrier function

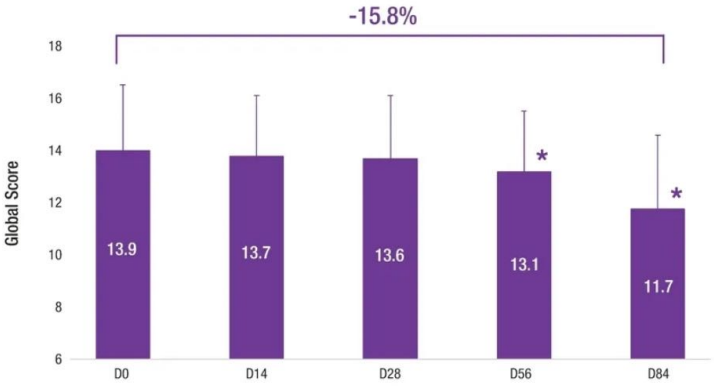
"There are [several] biologic pillars to target hyperpigmentation, and we do a better job when we target as many of these factors as possible," says Dr. Baldwin. "We're not going to pick one agent that does one thing. We are going to pick agents, or a combination of agents, that do several things."

Mela B3 serum offers a multi-pronged approach to managing dyspigmentation. The serum contains the active ingredient Melasyl, the antioxidant carnosine, hyaluronic acid, and glycerin. In addition, it contains lipohydroxy acid and retinyl palmitate, which exfoliate the surface of the skin and accelerate cell turnover and skin renewal. Ten percent niacinamide and cystoseira tamariscifolia, which suppress formation of excess melanin and decrease inflammation.

An emerging body of data is reinforcing the effectiveness of this novel cosmeceutical in managing hyperpigmentation. One three-month single-arm exploration involving 32 adults with phototypes III through VI with post-acne PIH who had less than nine acne lesions and a Post-Acne Hyperpigmentation Index (PAPHI) score of greater than 10, was conducted in Mauritius, a subtropical island country in the Indian Ocean. The PAPHI score is a composite of the size of lesions, the intensity of pigment within those lesions, and the number of lesions. The worst possible PAPHI score is 22, and the mean score at baseline in this study was 13.9.

Study participants applied the serum twice daily to their entire face for three months. Subjects in this study were not given any additional photoprotection in the form of sunscreen.

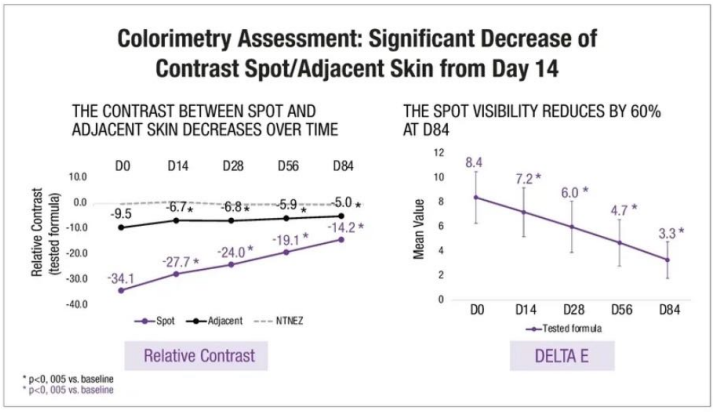
PIH Study Results: Significant Decrease of PAPHI Score From Day 56



* p<0, 005 vs. baseline

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"They really wanted to see what the Mela B3 serum was able to do on its own in terms of reducing hyperpigmentation," says Dr. Baldwin.

The PAPHI score steadily decreased, reaching statistical significance at Day 56. There was a 15.8% decline in the PAPHI score from baseline to Day 84, at which point the score was 11.7.

This study also measured colorimetry, which assesses the contrast between the spot and the adjacent skin. From Day 0 to Day 84, there was a progressive reduction in contrast between the spot and surrounding skin. Researchers noted a significant decrease in colorimetry, as early as 14 days after application of Mela B3. Measured by Delta E or the change in skin color induced by UV, spot visibility fell over time, decreasing by 60% after three months of Mela B3 use.

Many patients are concerned that treating dark spots may also affect normal skin tone. "This [study] suggests that we may be able to treat the whole face, not just lesional skin, and be able to get that evenness. That's what patients are looking for," says Dr. Alexis.

Ask the Expert

Q: Is Mela B3 sunscreen tinted?

A: "It is not tinted. It is white in color, but it blends in very easily with the skin. It isn't chalky or sticky."

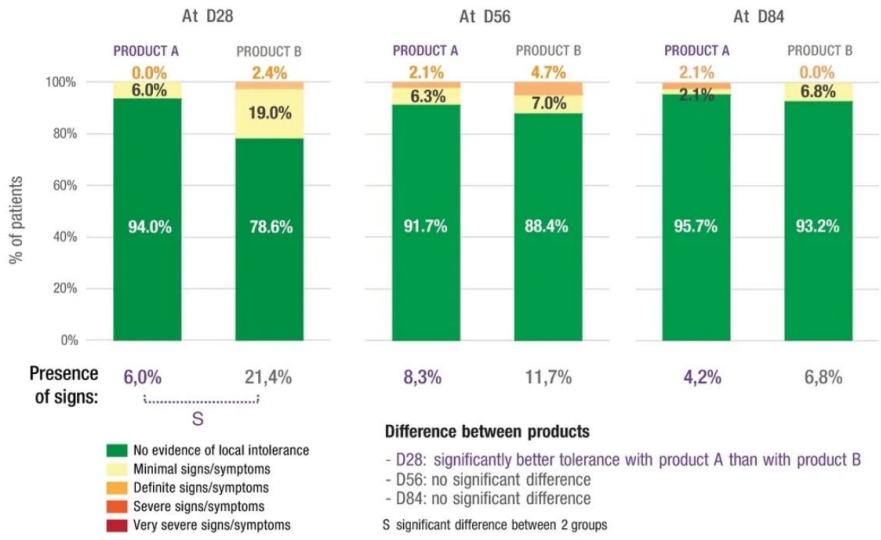
-Dr. Baldwin

"I've been very impressed with how easily it blends in, which is often a challenge… with darker skin phototypes. Even in very richly pigmented skin, such as type VI or I have noticed it blend in and be very cosmetically acceptable. It is important from an adherence point of view that if we want to get the best outcomes, we need our patients to use the products, including photo protection (products), regularly."

-Dr. Alexis

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Mela B3 also caused little irritation to subjects.

"Clearly these patients are getting better rapidly with twice-daily application, with really nothing in the way of irritation," says Dr. Alexis. "It's a win-win situation."

In a non-inferiority study of Mela B3 vs. 4% hydroquinone in melasma (mixed or dermal; mild, moderate, or severe), 102 adult females with skin phototypes I through IV applied Mela B3 twice a day, in the morning and at night, or hydroquinone once daily, at bedtime. All subjects applied a tinted sunscreen once in the morning and once at midday. Participants were assessed at baseline at Days 28, 56, and 84 for changes in the forehead, right and left malar regions, and the chin using the modified Melasma Area and Severity Index (mMASI), an ascending scale ranging from zero (no melasma) to 24 (severe melasma). There were no differences in the scores between the two arms. The mMASI score was 7.6 in the Mela B3 arm and 7.4 in the hydroquinone arm. In addition, there was no significant difference between the two arms when measuring change in mMASI score from baseline to Day 84 (-2.16 in the Mela B3 arm and -2.56 in the hydroquinone arm, respectively).

Moreover, the novel serum was better tolerated than hydroquinone. There was a statistically significant difference in local tolerance favoring Mela B3 at Days 28, 56, and 84. Mela B3 was found to be non-inferior to hydroquinone at improving quality of life on Days 28, 56, and 84.

In a single arm study of 60 adult women with skin phototypes IV through VI who had mild-to-moderate hyperpigmentation of various types or mild-to-moderate skin unevenness, the use of Mela B3 SPF 30 sunscreen significantly decreased skin roughness and enhanced overall skin appearance after two weeks. At the four-week mark, Mela B3 serum and sunscreen significantly improved uneven skin tone, hyper-

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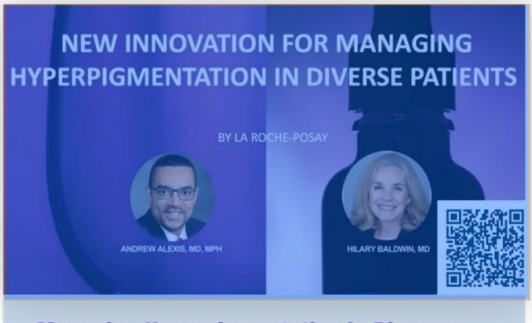
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pigmentation, and overall skin appearance and decreased dullness and roughness of the skin and fine lines.

In this study, the serum was applied once in the morning and once at bedtime, and the sunscreen was applied 15 minutes before sun exposure and re-applied as needed every two hours.

Conclusion

There is a high prevalence of pigmentary disorders in the population. More than just a cosmetic concern, the disorders also have a deleterious impact on quality of life and may result in social stigmatization. The latest innovation in managing hyperpigmentation disorders is Melasyl, which is found in Mela B3 serum and moisturizer. In particular, the serum has demonstrated robust efficacy and highly favorable tolerability in treating PIH. The novel ingredient has shown non-inferiority to hydroquinone 4%, with better tolerability and greater improvement in quality of life. Moreover, a regimen of Mela B3 serum and Mela B3 sunscreen (SPF 30) has demonstrated powerful efficacy in decreasing discoloration and improving skin texture in skin of color.



Managing Hyperpigmentation in Diverse Patients With MELA B3

Andrew Alexis, MD, MPH, and Hilary Baldwin, MD, discuss how La Roche-Posay's latest innovation, MelaB3 Serum, is changing the way they treat hyperpigmentation. Powered by Melasyl, this new multi-patented pigment-correcting serum reduces post-acne marks, sunspots, age spots, and even persistent dark spots across skin tones.

https://thedermdigest.com/videos/la-roche-posay-mela-b3-launch/

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