more accurate at skin cancer diagnosis than general practitioners and advanced practice physicians, as preliminary studies seem to suggest, prioritizing the performance of biopsies to dermatologists may be a highly cost-effective strategy. Further studies could also explore the effect of various interventions on improving the NNB, such as standardizing the use of dermoscopy and implementing additional training programs for general practitioners and advanced practice professionals.

## ARTICLE INFORMATION

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## NOTABLE NOTES

## The Quest for the Ultimate Skin-Lightening Agent

Samantha Hsieh, BS; Eric L. Maranda, BS; Tarek Salih, BS; Austin Nguyen, BS; Joaquin Jimenez, MD

Vulgar. Improper. Such was the prevailing view of makeup during the reign of Queen Victoria from 1837 to 1901. Makeup was meant only for actors and prostitutes. Women who openly dared to "paint" their faces were vilified. Natural remedies, including water and inner purity, were touted as the keys to achieving the Victorian archetype of beauty: pale skin devoid of blemishes.<sup>1</sup> Pale skin signified social status and distinguished the tanned working class who worked outside in the fields from the pale upper class who did not need to work.<sup>2</sup>

Nevertheless, many women—and even some men—in the Victorian era skirted around these societal restrictions by using "medicinal" cosmetics such as white powder to lighten their skin complexion.<sup>1</sup> The composition of the white powder varied from plain starch to talcum powder to hydroxide, carbonate, and lead oxide, which sometimes resulted in lead poisoning. Some Victorian women idolized a pale pallor so much that they even used arsenic to try and attain the whitest complexion possible, which occasionally led to death. A less toxic facial powder—zinc oxide—was eventually discovered in the 19th century, and it is still used today, especially in sunscreen.<sup>2</sup>

We now understand that human skin color is due to a pigment called melanin, which is produced by melanocytes in the stratum basale of the epidermis, the outermost skin layer. However, the desire for pale skin in the Victorian era continues to permeate throughout our society, especially in Asian and African countries where fairer skin is still associated with higher societal status. We continue to devise concoctions to whiten skin, though we now strive to target specific pathways of melanin production to depigment and thereby lighten skin color. For example, many whiteners act by inhibiting tyrosinase, a coppercontaining enzyme that catalyzes the first 2 steps of melanogenesis: the hydroxylation of L-tyrosine to L-dihydroxyphenylalanine (DOPA) and its subsequent oxidation to L-DOPAQuinone.<sup>3</sup> Other skin-bleaching agents aim to interfere with pathways such as melanosome maturation and transfer and melanocyte loss. These agents can be classified as botanicals, anti-oxidants, vitamins, peptides, or  $\alpha$ - and  $\beta$ -hydroxyl acids and derivatives. Other methods, including laser treatment, are also constantly being optimized for skin whitening.<sup>3</sup> In addition, these whitening regimens have therapeutic implications for various dermatological diseases including hyperpigmentation and vitiligo.

Yet despite these advances in pigment biology, the potencies and toxic effects of skin-lighteners are not well understood. Centuries after the Victorian era, the quest still continues for an effective and safe skin-lightening agent.

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