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The Medical Treatment of Vitiligo: An Historical Review



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KEYWORDS

• Vitiligo • Medical treatments • Psoralens • Ultraviolet light

KEY POINTS

- Vitiligo and other disorders causing white spots on the skin have been recognized for thousands
 of years.
- Vitiligo carries a heavy social burden resulting in banishment, inability to marry, and embarrassment.
- Investigators have sought treatments that range from burning to blistering to tattooing to relieve the suffering of those affected.
- Phototherapy, especially psoralens and exposure to ultraviolet A, have had a modicum of success in treating vitiligo.
- Many other oral and topical agents are used to minimize the scourge of vitiligo.
- Results of new research promise the possibility of a cure that would stop the progression of depigmentation and permit repigmentation in those affected.

You are not just white, but a rainbow of colors. You are not just black, but golden. You are not just a nationality, but a citizen of the world.

 Suzy Kassem, Rise Up and Salute the Sun: The Writings of Suzy Kassem

The color of human skin is remarkable for its breadth of color and fascinating for its science and biology.

It ranges from white, to yellow, to brown and even a dark, almost black.

Humans have used skin color to distinguish their nation, tribe, and even their family from other peoples, skin color often a designation of friend or foe. The science and biology of skin color remained a mystery until the early twentieth century when melanocytes were described and the chemistry of formation of melanin within the epidermis was worked out.

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HISTORY OF LEUKODERMA, WHITE SPOTS, AND VITILIGO

Perfect, flawless skin color is desired by everyone for its beauty and attractiveness. However, like all biologic systems, pigmentation can be abnormal. There can be dark spots or light spots, both of which are disfiguring. These problems have caused distress to people for millennia. Already in 1500 to 1000 BCE, Indian writers described "kilas" and "palita," translated as white or yellowish white spots.3 The Ebers Papyrus describes people with white spots. In these early writings, the precise condition being described is not known, although leprosy and vitiligo are just two of many possible candidates. There are numerous references to white spots in the Old Testament. Typically these were considered leprosy but it is plausible that much of what was considered to be leprosy was vitiligo or other disorders of skin color. 4 In the Far East prayers known as Makatominoharai dating from 1200 BCE recognized white skin, possibly vitiligo.⁵

In the sixteenth century, Hieronymus Mercurialis⁶ published his book on diseases of the skin. In it he devotes an entire chapter, entitled "On Leuce and Alphos," to disorders of abnormal skin color. He cites early Arabic, Greek, and Latin scholars about white spots and notes that the word

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"...'vitiligo' is a Latin word derived from either 'vitium' (blemish) or 'vitulum' (small blemish)..." The word vitiligo might have been first used by Celsus. Mercurialis suggests that phlegm accumulating under the skin was the source of leukoderma, a theory that he confirms from the writings of "...divine Plato...that white phlegm has two effects in the body....if it begins to vent through the exterior of the body, it will cause ...vitiligo." Herodotus in Greece noted white spots on foreigners and suggested they be banished immediately, their having sinned against the sun. 5

In China and Korea, writers discussed white spots and white skin. In Korea vitiligo and other pigmentary disorders, such as nevus depigmentosus or tinea versicolor, were described in Doney Bogam, published in the seventeenth century.⁵ A portrait of Chang-Myeong Song, a high ranking official of the Yi dynasty of Korea, was painted about this time that shows the typical depigmentation of vitiligo.⁵

In the seventeenth century, William Byrd⁸ described "An Account of a Negro-Boy that is, dappel'd in several places of his Body with White Spots." The depigmentation began at age 3 years and continued to spread. Byrd conjectures that in time the boy would become all white. The leukoderma was obviously mysterious in origin.

Brito⁹ in the nineteenth century discussed vitiligo. He emphasized the social stigma of white spots and their capacity to disfigure. "The appearance of the unfortunate victims of vitiligo is striking, and scarcely fails to evoke a feeling of horror and pity for the afflicted,...The picture of otherwise dark person,...marked with spots perfectly white,...to even eyes familiarized to the sight, appears repugnant."

The worldwide distribution of these reports dating back thousands of years attests that vitiligo was and is ubiquitous. The comments of some of the previously quoted authors confirm its deleterious effects on those who suffer from it. It is often said that vitiligo is only a cosmetic problem. It is not entirely true that vitiligo does not affect the physical functioning of the body in any detrimental way. There are pigment cells in organs and tissues other than skin, such as the eye, inner ear, and leptomeninges. 10 Vitiligo can affect choroidal melanocytes and retinal pigment epithelium causing iritis and chorioretinitis. 11-13 Voqt-Koyanagi syndrome is characterized by unilateral vitiligo, poliosis, meningitis, and dysacusia, probable manifestations of melanocyte destruction in each of these organs and tissues. 11 These extracutaneous manifestations of vitiligo rarely cause loss of visual acuity or hearing. Regardless vitiligo like albinism causes immense social, emotional, and personal pain and disability. Even

today in the middle east, young people with vitiligo find it an impediment to finding a marriageable partner. The plethora of treatments (**Table 1**) proposed and tried for thousands of years attest to its significance in all cultures and societies. Its detrimental effects on quality of life have now been thoroughly studied and are well characterized. ^{14,15}

STUDY OF SKIN COLOR AND WHITE SPOTS

Skin color was a mystery until modern times after the invention of the microscope, the techniques

Table 1 Historical treatments for vitiligo

Levamisole Agaric, turpeth, and Mefloquin colocynth Melaginina Anapsos Methotrexate Anthralin Minigrafting autografts Minoxidil Arsenic Monoamine oxidase **Aspirin** Bergamot inhibitors Bavachee seeds Monobenzyl ether of Bitter almonds in hydroquinone vinegar Mustard Byzantine syrup Oxymel Cantharidin Pimecrolimus Carmustine (BCNU) Phenylalanine-Clofazimine ultraviolet A Psoralens + sunlight Chloroquine Psoralens + ultraviolet A Copper Corrosive sublimate Pseudocatalase Cosmetics Ouinacrine Crude coal tar Resorcin paste Rose-flavored honey Cryotherapy Cyclophosphamide Selective diets Steroids oral or topical Cyclosporine Dapsone Surgical excision Dermabrasion Syrup of betony Dopa oral and **Tacrolimus** Tattooing topical **Escharotics** Thermal and caustic Finsen lamp blistering Fluorouracil Tincture of nux vomica Fluphenazine Tretinoin enanthate Ultraviolet B narrow Folic acid band Hydrochloric acid Vesicants Hydrogen peroxide Vibrapuncture Injections of silver Vitamin B₆ nitrate Vitamin B₁₂ Vitamin C Vitamin D Isoprinosine

Adapted from Montes LF. Vitiligo: current knowledge and nutritional therapy. 3rd edition. Buenos Aires: Westhoven Press; 2006.

Vitamin E

Khellin oral and

topical

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