Melasma Myths

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Melasma is an acquired, symmetric hypermelanosis of the face that presents as light to dark macules and patches. The pathogenesis of this pigmentary disorder is still not completely understood. Some concepts about the disease are based more on mythology than on scientific evidence. The objective of this article is to discuss the myths associated with melasma.

During the last 20 years, a small number of studies have been conducted to determine the etiology of melasma. A better understanding of the pathogenesis of melasma could lead to the development of more specific therapies.

A myth is defined as an ill-founded belief held uncritically or a traditional story of ostensibly historical events that serves to unfold part of the world view of a people or explain a practice, belief, or natural phenomenon. This article discusses 7 myths associated with melasma.

Myth 1: Dermal and mixed melasma are clinicopathologic variants of melasma.

Few studies evaluating the histopathologic characteristics of melasma have been published in the literature. Sánchez et al[1] reported on a clinicopathologic study of 76 Puerto Rican women with melasma. Of these, only 17 subjects underwent skin biopsies. Based on clinical and Wood's lamp examination, as well as histopathologic findings, investigators classified melasma into 4 types: epidermal, dermal, mixed, and Wood's light inapparent. Histopathologically, epidermal melasma was characterized by an increase in melanin deposition in the basal, suprabasal, and, occasionally, upper epidermal layers. Dermal melasma was characterized by a similar (though not as prominent) epidermal hyperpigmentation, but melanin-laden macrophages were noted perivascularly in the superficial and deep dermis. A numeric quantification of these macrophages was not reported. Examination of normal skin showed "slight" melanization of keratinocytes in the basal layer and other keratinocytes.

Kang et al[2] conducted a clinicopathologic study of 56 Korean women with melasma. Two-millimeter punch biopsies were performed on lesional and adjacent (1 cm) skin of all study participants. Melanin deposition in all epidermal layers and the degree of solar elastosis increased significantly ($P<.05$) in lesional compared with perilesional skin. Nevertheless, dermal melanophages were confined to lesional skin in only 3 subjects (5%). Dermal melanin was present in both lesional and normal skin in 20 subjects (36%). Of these 20 subjects, only 4 (20%) showed more dermal melanophages in lesional than in normal skin. Overall, only 7 subjects (13%) showed increased dermal melanin and melanophages in lesional skin. Ultrastucturally, dermal melanophages were variably distributed in both lesional and normal skin. Based on these findings and the fact that melanophages are known to be present in the dermis of Korean persons with normal skin, Kang et al[2] concluded that melanophages cannot be a hallmark of dermal melasma and suggested that there is no true dermal type of melasma.

In accordance with the data collected by Kang et al,[2] Sánchez et al[1] described a "small" number of melanin-laden macrophages present in the papillary dermis of patients with epidermal melasma. Clinically, these results suggest that the hyperpigmentation seen in melasma lesions is independent of the presence or absence of dermal melanophages (Figures 1 and 2). It is possible that the different degrees of hyperpigmentation seen in melasma lesions may correlate only with the total amount of melanin in the epidermis. Another explanation may be that the degree of pigmentation in a given melasma lesion may reflect contributions from both an increased amount of epidermal melanin and a constitutive presence of a racially or genetically determined number of dermal melanophages. To the best of our knowledge, a descriptive and/or quantitative histopathologic study on the presence of dermal melanophages in normal facial skin of Hispanics has not been published. Such studies are

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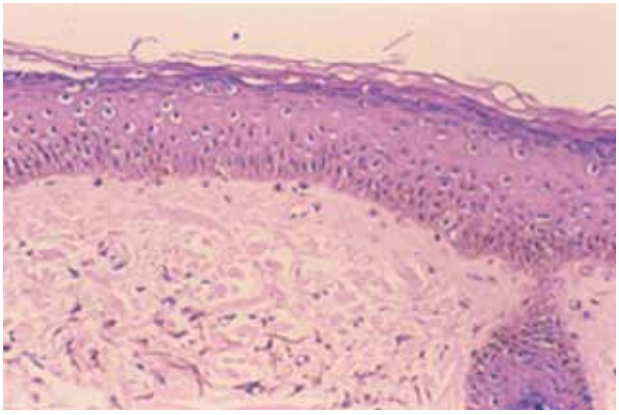

Figure 1. Melasma. Increased melanin deposition in the epidermis and melanophages in the papillary dermis (H&E, original magnification ×20).

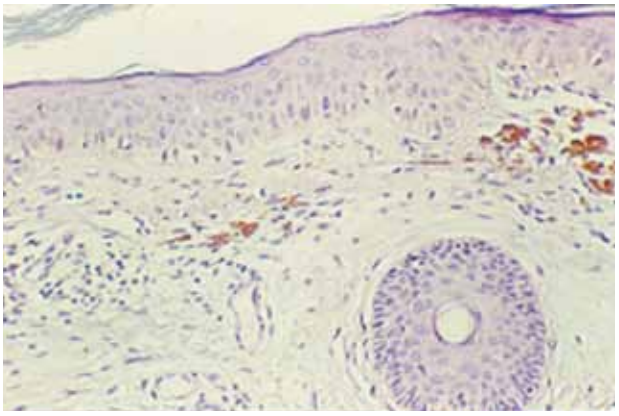

Figure 2. Normal skin adjacent to melasma lesion. Note the presence of melanophages (H&E, original magnification ×20).

necessary to accurately assess any actual difference in the population of dermal melanophages in melasma lesions compared with perilesional skin. Additional larger controlled studies are needed to confirm the results of Kang et al.[2] In the meantime, classifying melasma lesions as dermal or mixed may be misleading.

Myth 2: Mandibular melasma is a clinical variant of melasma.

Three clinical patterns of melasma have been recognized: centrofacial, malar, and mandibular.[1] The centrofacial pattern involves the cheeks, forehead, upper lip, nose, and chin; the malar pattern involves the cheeks and nose; and the mandibular type involves the ramus of the mandibula and the lateral aspects of the face and occasionally may extend to the neck (Figure 3).[3]

Mandry Pagán and Sánchez[3] evaluated 10 women with mandibular melasma to compare its clinical and histopathologic characteristics with centrofacial and malar melasma (mean age, 52 years; mean age of onset, 40 years). By comparison, centrofacial melasma usually occurs during childbearing years (mean age of onset, 29 years). In the study population, the clinical presentation of mandibular melasma was characterized by the presence of confluent hyperpigmented patches localized to the mandibular region, often extending to the cheeks. A history of chronic sun exposure was a common factor among the study participants. Histopathologic examination revealed an increase in epidermal pigmentation in the basal and suprabasal layers. In addition, most biopsy specimens (80%) showed histopathologic evidence of sun damage—namely solar elastosis, epidermal atrophy, telangiectases, and dermal melanophages.[3] These findings, similar to those of poikiloderma of Civatte,[4] have not been described in centrofacial or malar melasma. Mandry Pagán and Sánchez[3] suggest that mandibular melasma may represent a distinct clinicopathologic entity, perhaps a variant of poikiloderma of Civatte (eg, acquired brachial cutaneous dyschromatosis,[5] melasma of the arms[6]).

Myth 3: Estrogens are important in the pathogenesis of melasma.

Melasma is commonly observed in pregnant women, women using oral contraceptives, and postmenopausal women on hormone replacement therapy. For this reason, increased estrogen levels have frequently been implicated as a major etiologic factor in the development of melasma. Nevertheless, studies evaluating hormonal status in women with melasma fail to show a direct relationship between the condition and increased plasma estrogen levels. Perez et al[7] performed an extensive hormonal evaluation of 9 nulliparous women with idiopathic melasma and found them to have significantly elevated plasma levels of luteinizing hormone (LH) and decreased levels of estradiol ($P<.001$ and $P<.025$, respectively) compared with control subjects. The investigators theorized that a mild subclinical ovarian dysfunction may underlie some cases of melasma. Based on the known capability of keratinocytes and skin fibroblasts to metabolize steroid hormones,[8] the investigators commented on the possible presence of locally produced active hormones in the skin (such as estrogen), which may, in turn, influence the development of melasma. They also suggested that an increase in the number or sensitivity of estrogen receptors in the skin and/or hypothalamopituitary area may play a role in this condition.

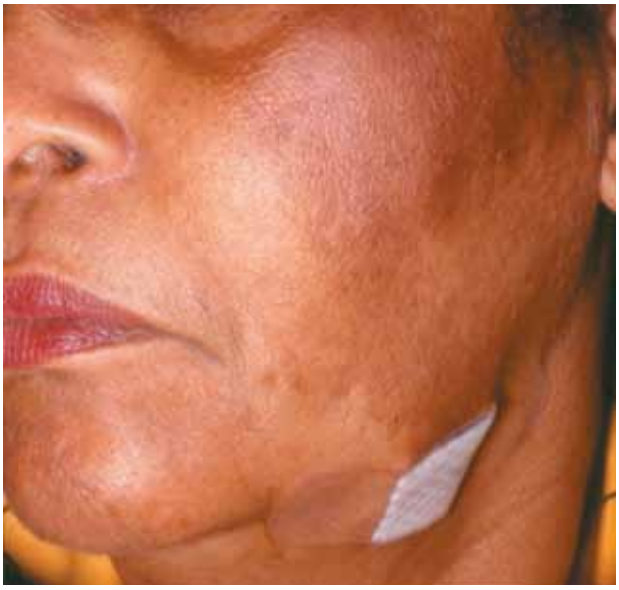

Figure 3. Mandibular melasma.

Hassan et al[9] evaluated 36 women with melasma and found elevated levels of LH, follicular stimulating hormone, and estradiol, and low levels of prolactin compared with control subjects. Twenty-six of the study participants (72%) did not report any relationship between prior pregnancies and melasma. The investigators proposed that increased estrogen levels may help maintain melasma.

Sialy et al[10] reported on 15 men with melasma who were found to have increased LH levels and decreased testosterone levels compared with age-matched control subjects, though the levels were within the normal expected range values. The investigators thus concluded that a subtle testicular resistance may be involved in the pathogenesis of melasma in men.

In a study by Lutfi et al,[11] the frequency of thyroid disorders in women with melasma was 4 times greater than control subjects. Furthermore, 70% of women who developed melasma during pregnancy or while using oral contraceptives had thyroid abnormalities compared to 39.4% of female subjects with idiopathic melasma. The investigators suggested that estrogen may serve as a trigger for the development of melasma in women who are predisposed to thyroid abnormalities. These data may suggest that genetic factors, specifically related to autoimmunity, may be more important in the etiology of melasma than elevated estrogen levels alone. Estrogen levels were not measured in this study.

Further evidence against the possible role of estrogen in the pathogenesis of melasma is the fact that only a small percentage of pregnant women (8%) or women using oral contraceptives (29%) develop melasma.[9,12] In addition, melasma does not always resolve once estrogen levels return to normal (ie, after pregnancy or discontinuation of oral contraceptives). In a study by Sánchez et al,[1] only 30 of 76 women (39%) with melasma developed the condition after taking estrogen/progesterone pills or during pregnancy. In addition, 30% of women who developed melasma during pregnancy still had the disorder 10 years after gestation.[13]

Sánchez et al[14] found that melasma due to pregnancy or oral contraceptives is more common during the summer months and in southern latitudes, suggesting that UV exposure is an important etiologic factor. The greater incidence of melasma in heavily pigmented races living in sunny, tropical areas such as Puerto Rico is contrasted by its low incidence in Swedish women. Thus, UV light appears to be more important than estrogen in the etiology of melasma.

In summary, the published scientific data do not establish a direct link between high estrogen levels and the development of melasma. Rather, results from 3 studies indicate that possible subtle hormonal alterations manifested by increased levels of LH contribute to the pathogenesis of melasma.[7,9,10] Although high plasma estrogen levels are not directly correlated with melasma, some authors comment that increased local estrogen production or increased estrogen receptor sensitivity in the skin may play a role in its pathogenesis. However, no data have been published to support this assertion, and other factors such as UV exposure seem to be more relevant than estrogen in the development of melasma.

Myth 4: The Wood's lamp is useful in determining the appropriate therapy for melasma.

The Wood's lamp, developed by Robert W. Wood in 1903,[15] is a useful diagnostic tool for a variety of metabolic, infectious, and pigmentary dermatologic conditions. The original Wood's lamp was a medium-pressure mercury lamp with a glass envelope, fitted with a nickel–chromium oxide–silica glass filter. This device was capable of emitting long-wave UV radiation in the 320- to 420-nm range of the electromagnetic spectrum, with a maximum output at 365 nm. Newer versions consist of low-pressure UVA-emitting fluorescent lamps with a UVA-transmitting visible-absorbing glass envelope. The radiation spectrum of the Wood's lamp, the light-absorbing properties of the skin, and the absorption spectra of melanin make this device suitable for evaluation of pigmented skin lesions.

Wood's lamp illumination of a hyperpigmented lesion of epidermal origin such as a freckle will demonstrate enhancement of color contrast between the lesion and the surrounding unaffected skin. If the pigmented lesion is of dermal origin such as nevus of Ota, illumination with the Wood's lamp will fail to show enhancement or accentuation of color contrast.

Some believe that Wood's light examination of pigmented lesions in patients with dark skin (Fitzpatrick skin types IV and V) is of no value because of optical factors associated with an increased melanin deposition in all the layers of the epidermis.[16] These patients would be classified as Wood's light inapparent.[1] Since melasma is more prevalent in dark-skinned individuals (ie, Fitzpatrick skin types IV–VI)[17] of Hispanic or Asian origin,[18,19] it is likely that many affected patients will not benefit from a Wood's light examination.

Lawrence et al[20] evaluated the efficacy of the combined peel (70% glycolic acid versus Jessner solution) and topical therapy (0.05% tretinoin and 4% hydroquinone) using a split-face approach for the treatment of 16 women with melasma. They also assessed the reliability of the Wood's light examination in predicting a response to treatment. Out of 4 patients with nonenhancing lesions on Wood's light examination, 2 had a partial response, 1 had an excellent response, and 1 worsened with treatment. Of the 12 patients with Wood's light–enhancing lesions, 5 had an excellent response, 6 had a partial response, and 1 had a negative response. The investigators concluded that Wood's lamp examination did not help predict the clinical response to peels "as clearly as anticipated."[20]

Considering the possibility that all melasma cases are "epidermal," Wood's light examination to determine the distribution of melanin within lesions may prove to be of little value. In addition, dark skinned patients with melasma (Fitzpatrick skin types IV and V) will not benefit from Wood's light examination. Published data on the predictive value of Wood's light examination for clinical efficacy of therapeutic measures has proven to be, at best, limited.

Myth 5: Retinoids alone are effective in the treatment of melasma.

Melasma is a challenging condition to treat. Multiple factors, such as genetics, hormones, and UV radiation, have been implicated in its pathogenesis.[1] Different topical agents, including hydroquinone, sunscreens, tretinoin, corticosteroids, glycolic acid, and azelaic acid, have been used for the treatment of melasma, demonstrating some benefit either as monotherapy or in combination. Kligman and Willis[21] were the first to describe the use of tretinoin in the treatment of melasma. They designed a depigmenting formula consisting of 0.1% tretinoin, 5.0% hydroquinone, and 0.1% dexamethasone in a hydrophilic ointment or ethanol-polypropylene glycol solution. Kligman and Willis discussed possible mechanisms of action of tretinoin in melasma—namely dispersion of pigment granules in keratinocytes, interference with pigment transfer, and acceleration of epidermal turnover. They also postulated that tretinoin may act merely as an irritant. None of these agents was found to be as effective alone as when used in the triple combination.[21] To establish the efficacy of topical retinoids, a review of the few controlled studies evaluating these agents alone versus vehicle is appropriate.

Griffiths et al,[22] in a 40-week clinical trial of 38 subjects with melasma, observed a significant improvement ($P<.0006$) in subjects treated with tretinoin and sunscreen compared with those treated with vehicle and sunscreen. Initial clinical response was noted after 24 weeks of active treatment.[22] In a similar study, Kimbrough-Green et al[23] reported the efficacy of topical 0.1% tretinoin in a 40-week double-blind clinical trial of 28 black patients with melasma. Again, an improvement ($P<.05$) in the active treatment group was noted as compared with the vehicle-treated group.

In contrast, Tadaki et al[24] treated 8 patients with melasma and 3 patients with xeroderma pigmentosum with 0.1% tretinoin cream for 6 months. All patients showed improvement in fine surface lines in the periorbital region, but no significant improvement in melasma was observed. Interestingly, there is a report of a 34-year-old female patient who started isotretinoin therapy for severe acne and developed a melasmalike pigmentation on her face after 4 weeks of therapy.[25] A similar dyschromia had been reported during her first pregnancy, which resolved with the use of broad-spectrum sunscreen 1 month after delivery. The patient completed a 6-month course of isotretinoin, and the pigmentation resolved 1 month after discontinuing therapy. The author commented that 60 other similar occurrences had been reported either to the manufacturer or to the Committee on Safety of Medicines.[25]

The published literature evaluating the efficacy of topical retinoids as monotherapy for the treatment of melasma is limited and presents conflicting results. When effective, the onset of action is slow (24 weeks), and local side effects can be troublesome. Nevertheless, the positive role of retinoids as adjunctive treatment to other topical

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therapies such as hydroquinone and topical corticosteroids for the treatment of melasma has been documented. Larger controlled studies are needed to determine the precise role of topical retinoids as monotherapy in the treatment of melasma.

Myth 6: Abrasion techniques are effective in the treatment of melasma.

Abrasive procedures such as chemical peels, microdermabrasion, dermabrasion, and laser resurfacing have become very popular in the treatment of photoaging, pigmentary disorders, acne scars, and wrinkles. All of these procedures have been used in the treatment of melasma with variable results. Because a large percentage of patients with melasma have darker skin tones (Fitzpatrick skin types IV and V), both superficial and mid-depth abrasive agents should be used with extreme caution. Patients with dark pigmentation are prone to develop adverse reactions such as pigmentary (hyperpigmentation or hypopigmentation) or textural changes (hypertrophic scars or keloids) following these procedures.

Although there are many studies that suggest the efficacy of different peeling agents in the management of melasma, either alone or in combination with topical agents like hydroquinone, only a few controlled studies have been published. Giannotti and Melli[26] concluded that trichloroacetic acid peels are not very effective for treating melasma. In addition, they stated that the results obtained are inconsistent and the treatment may actually worsen the patient's condition. Katsambas and Antoniou[19] mention that chemical peels "sometimes stimulate melanogenesis, resulting in a worsening of the hyperpigmented patches." Sarkar et al[27] reported on 40 Indian patients with melasma treated with a modification of the formula designed by Kligman and Willis[21] and a broad-spectrum sunscreen. Twenty of these subjects also received a series of glycolic acid peels at 30% and 40%. Although both groups demonstrated significant improvement in melasma ($P<.01$), the subjects receiving glycolic acid peels experienced a slightly greater reduction in pigmentation than control subjects (79.99% vs 63.14%, respectively) at the end of the study. Hurley et al[28] conducted a randomized, controlled, split-face prospective trial of 21 Hispanic women with moderate to severe melasma. All subjects applied a 4% hydroquinone cream twice daily to both sides of the face and used a sunscreen with a sun protective factor of 25. One half of the face was treated with a series of 20% and 30% glycolic acid peels. Both sides of the face showed a significant improvement in melasma ($P<.001$), but the difference between the peeled and control sides did not reach statistical significance. The authors concluded that the use of "low-strength"[29] glycolic acid peels does not enhance the hypopigmenting effects of hydroquinone.

Although microdermabrasion is extensively used either alone or as an adjunct treatment in the management of melasma, studies evaluating its clinical efficacy in melasma are lacking. Alam et al[30] reported a right-left comparison of low-strength glycolic acid peels versus low-intensity microdermabrasion in 10 subjects with photoaging. Although the term *melasma* was not mentioned, there was minimal (if any) improvement in facial "brown spots" as evaluated by both the subjects and the investigators with either procedure. Shim et al[31] commented that "results with melasma are also inconsistent" and "microdermabrasion, however, should improve the penetration of other adjuvant topical medications for melasma." Bernard et al,[32] in a review of microdermabrasion, commented that "microdermabrasion is not effective for deep wrinkles and scars, ice pick–type acne scars, melasma, and postinflammatory hyperpigmentation."

Kunachak et al[33] reported a follow-up study of 410 subjects with melasma who underwent dermabrasion with a rotatory diamond fraise. Although 97% of the subjects had persistent clearance of their melasma (mean follow-up, 5 years; range, 1–9 years), 40% developed temporary hyperpigmentation and 35% developed temporary hyperemia several weeks after the procedure. The hyperpigmented lesions lightened in all subjects following the use of hydroquinone or topical corticosteroids for 4 to 6 months after the procedure. Two subjects developed hypertrophic scars, one subject experienced hypopigmentation, and some subjects developed milia following the procedure.

Manaloto and Alster[34] reported on 10 female patients (Fitzpatrick skin types II–V) with refractory melasma (ie, unresponsive to bleaching creams, chemical peels, and topical retinoic acid) treated with 3 full-face passes with an erbium:YAG laser. A significant improvement ($P<.0277$) seen during the first 10 days posttreatment was followed by postinflammatory hyperpigmentation in the majority of subjects 3 weeks posttreatment. Biweekly glycolic acid peels (30%–40%), topical suncreens, and azelaic acid were needed to restore the original posttreatment results by 6 months. Two small studies evaluating the treatment of melasma with combined ultrapulse CO_2 and Q-switched alexandrite lasers have been reported in the literature.[35,36] Although the combined laser treatment appeared to produce better responses than either laser treatment alone, some subjects (especially those with

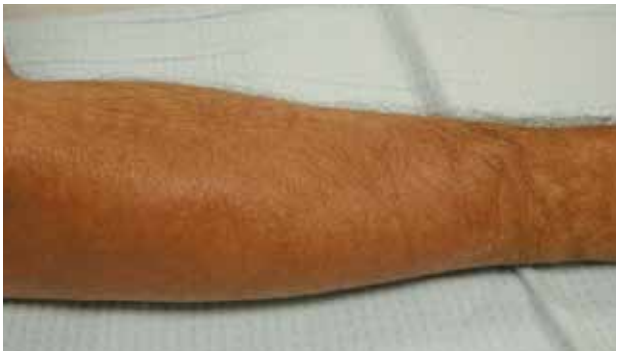

Figure 4. Hyperpigmentation of the forearm (arguably melasma).

Fitzpatrick skin types IV and V) developed postinflammatory hyperpigmentation that necessitated the use of topical bleaching agents.

Although abrasive procedures commonly are performed in patients with melasma, the available scientific data in certain cases are contradictory and, in many cases, limited. A major drawback to abrasive procedures for melasma is the fact that a large number of affected patients have darker skin, making them poor candidates for treatment because of the increased risk of postinflammatory hyperpigmentation.

Myth 7: Hyperpigmentation on the forearms is melasma.

Melasma of the forearms represents a clinicopathologic pigmentary disorder characterized by the presence of a macular brownish pigmentation mostly localized to the sun-exposed areas of the forearms (Figure 4). Twenty-nine cases[5,6,37,38] have been reported in the literature. The majority of affected patients are postmenopausal women on hormone replacement therapy, although 2 men with the condition have been described.[5,37] Whether this hyperpigmentation can be diagnosed as melasma is debatable. Patients with hyperpigmentation on the forearms rarely develop facial melasma, and no relationship to high levels of estrogen or pregnancy has been found. O'Brien et al[37] reported on 7 patients with hyperpigmentation of the forearms, most of whom did not have melasma at all or had only minor facial melasma during pregnancy or oral contraceptive use. Histopathologic examination revealed an increase in basal layer melanin. The authors believe that a pool of estrogen-sensitive melanocytes exists on the outer forearms, which mature later in life than those on the face.

Rongioletti and Rebora[5] described 20 patients with a brachioradial gray-brown pigmentation with hypopigmented, slightly atrophic macules scattered among the pigmented patches. Histopathologic findings on the 20 patients included increased basal layer pigmentation, epidermal atrophy, solar elastosis, and telangiectases. They differentiated this clinical presentation from other conditions such as melasma, poikiloderma of Civatte, dyschromatosis symmetrica, prurigo pigmentosa, macular amyloidosis, or prurigo melanotica and coined the term *acquired brachial cutaneous dyschromatosis* to describe this condition. Whether the condition described by Rongioletti and Rebora[5] is the same as the one described by O'Brien et al[37] and Johnston et al[6] deserves further study. Although Rongioletti and Rebora[5] differentiate acquired brachial cutaneous dyschromatosis from poikiloderma of Civatte, we still believe that this condition may represent a variant of poikiloderma of Civatte.

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