Definition of Melasma

Melasma comes from the Greek word “black-spot”. It is an acquired light-dark brown hyperpigmentation that affects sun-exposed areas such as the face and the neck.

Melasma, also known as chloasma, is a relatively common acquired, symmetrical hyperpigmentation or melanosis that classically develops on the sun-exposed areas of skin and frequently on the face and neck. Melasma conventionally refers to any generalized form of facial hyperpigmentation, resulting in either from inflammation or
medication use.

Epidemiology of Melasma

The disease is more common among young adults with females being affected more than males.

Women in the reproductive age are more commonly affected with a prevalence of 50 - 70%, whereas, only 20 - 25% of all cases are seen in men. It is commonly seen in the age group of 20 - 40 years, but it could start in childhood. Dark complexioned individuals (Fitzpatrick skin types III and IV), Asian and Hispanic females are more likely to develop this condition.

Etiology of Melasma

The exact etiology is unknown, but the nomenclature is most aptly used to describe the pigmentation associated with pregnancy. Various factors have been implicated as causative factors which include:

1. Sun exposure (ultraviolet radiation)
2. Genetic predisposition
4. Hormonal changes
5. Thyroid disease

Sun exposure

Sun exposure is the main factor for melasma. The risk of melasma increases with increasing sun exposure. The probable underlying cause is the over-production of melanin by melanocytes that have become hyper-functional. Ultraviolet rays from sunlight lead to the stimulation of melanocytes irrespective of the amount of sun exposure; thus, the incidence of melasma is highest in the Asian, African American and Hispanic or Latino women, especially during the summer season.

Pregnancy and Hormonal changes

When melasma is seen in pregnant women, it is known as chloasma or mask of pregnancy. Chloasma (chloazein) is a Greek term that means ‘to be green,’ while melasma (melas) is also a Greek term meaning ‘black.’ Melasma is the preferred term as the pigmentation is brown or black, rather than green. Apart from pregnancy, exposure to exogenous estrogen and progesterone due to ingestion of either oral contraceptives or hormone replacement therapy may also cause melasma.

In the case of exogenous hormones, the combination of estrogen and progesterone has been associated with pigmentation. Estrogen replacement therapy alone, without progesterone, does not precipitate melasma.

Idiopathic

Rare cases of idiopathic melasma have also been described in females and less commonly in males. In these cases, significantly elevated levels of the luteinizing hormone have been identified in both sexes, with an associated decrease in serum
estradiol in females and serum testosterone in males. The elevated levels of luteinizing hormone, along with reduced serum estradiol, are suggestive of mild ovarian dysfunction in females.

Thyroid disorders

Underlying autoimmune thyroid disorders, such as hypothyroidism, is considered as an aggravating factor in the pathogenesis of pregnancy-associated melasma.

Drugs

Photosensitizing drugs and phenytoin are risk factors that are under study.

Pathophysiology of Melasma

The production of melanin takes place in the melanocytes. The storage of this pigment further is in the melanosomes present within the keratinocytes. The skin color is determined by the number of melanocytes, the melanin content, as well as their location. Melanosomes also contain a copper-containing enzyme, tyrosinase. The role of this enzyme is to catalyze the conversion of L-tyrosine to L-dopa and L-dopa to L-dopa-quinone in the process of melanin synthesis.

A dysfunction in the above described pigmentary system leads to melasma, which is characterized by an irregular brownish or grayish-brown hypermelanosis of the face.

The most common theory is that in people who are predisposed to the development of melasma such as due to their skin type or genetic predisposition. Environmental influences such as sun exposure, hormone changes or medication use trigger the increased production of melanin leading to hyperpigmentation.

Most of the times exposure to sunlight is the most common cause leading to stimulation of a melanocyte-stimulating hormone, corticotrophin, and IL-1 all which increase the production of melanin.
Morphology of Melasma

Melasma appears in adult women as bilateral, light to dark brown, blotchy cutaneous macules that are either confluent with surrounding normal skin or are punctuate. They vary in size from a few millimeters to more than 2 cm in diameter. The lesions are sharply marginated and roughly symmetrical.

Commonly affected areas are mid-face, forehead, upper lip and chin. In many cases, the entire face is also involved. Certain individuals get patches on forearms and neck; however, this is rare. In females, the lesions are spread centrofacingly and over the mandibular region, while in males, lesions over the malar region are more common.

Various patterns of lesions are:

- **Centrofacial lesions** — wherein the pigmentation is spread over the forehead, nose, cheeks and upper lips.
- **Malar pattern** — wherein pigmentation is seen only over cheeks and nose spreading in a horizontal fashion.
- **Lateral cheek pattern**
- **Mandibular pattern** — wherein lesions are seen along the lower jawline.
- **Branchial pattern** — wherein the upper arms and shoulders are involved.
- There can be inflamed forms of melasma known as *erythrosis pigmentosa faciei*.

The pigmentation may remain faint or darken with time. Melasma generally has a rapid course evolving over a few weeks, and this differentiates it from other types of diffuse melanosis. Sun exposure is considered as an exacerbating factor as the lesions develop slowly with sun exposure.

Classification of Melasma
Melasma has been classified based on the depth of melanin pigmentation. The depth of the melanin pigment can be identified with the help of Wood’s Lamp. Wood’s Lamp emits black light containing UVA1. This classification, therefore, helps in the prediction of the treatment outcome. The classification scheme follows:

<table>
<thead>
<tr>
<th>Type of melasma</th>
<th>Color of lesions under normal light</th>
<th>Clinical features</th>
<th>Prognosis after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermal</td>
<td>Light brown</td>
<td>Well-defined borders</td>
<td>Good</td>
</tr>
<tr>
<td>Dermal</td>
<td>Bluish gray</td>
<td>Ill-defined borders</td>
<td>Poor</td>
</tr>
<tr>
<td>Mixed</td>
<td>Dark brown</td>
<td>Most common type showing mixed pattern</td>
<td>Partial</td>
</tr>
</tbody>
</table>

Diagnosis of Melasma

The diagnosis of melasma is mainly based on clinical examination and a correlation with the history given by the patient. However, sometimes additional diagnostic aids are needed for a confirmatory diagnosis. These are:

1. **Dermoscopy** is one of the aids useful in the diagnosis of melasma. Various shades of pigmentation can be seen using dermoscopy which can be further correlated with the type of melasma.

2. **Reflectance confocal microscopy (RCM)** is a non-invasive technique with the help of which skin layers up to the papillary dermis can be studied and images can be obtained that are similar to histopathological examination.

3. **Skin biopsy**: Histopathologically, melasma is characterized by increased melanin deposition or melanosis within an otherwise unremarkable epidermis. There is no increase in the number of melanocytes, but the size of melanocytes may be larger than those present in the adjacent normal pigmented areas. The pigment may also be seen within numerous melanophages in the dermis.
Treatment of Melasma

The lesions of melasma may spontaneously resolve after parturition or soon after cessation of exogenous hormones or regulation of endogenous sex hormone levels. There is no potential for malignant transformation. Treatment of melasma is exigent due to the dermal component and a propensity for relapse.

The goals of treatment are:

- Lightening of skin color
- Reduction in the size of the affected area
- Prevention or reduction of recurrence of the lesions
- Providing a cosmetically acceptable effect
- Reducing the time to clearance

These can be achieved with the fewest possible side effects by:

- Achieving inhibition of melanocyte activity and melanin synthesis.
- Disruption and removal of melanin granules.
- Killing of melanocytes.

The following treatment options are currently used and much more are under study:

Medications

Medications are the primary line of treatment and are available in the form of creams, lotions, gels or liquids. The first line therapy which is the most efficacious consists of a triple combination topical therapy consisting of 4% hydroquinone, 0.05% tretinoin and 0.01% fluocinolone acetonide. Dual ingredient topical agents include hydroquinone combined with glycolic acid or kojic acid. Single topical agents such as 4% hydroquinone, 0.1% retinoic acid or 20% azelaic acid are alternatives for patients who are sensitive to triple combination therapy. These medicines, however, have side-effects such as skin irritation and darkening of the skin etc. in a few patients.


Hydroquinone is considered as the gold standard in the treatment of melasma when used in the concentration of 2 - 4%. It causes inhibition of the tyrosinase enzyme, thereby preventing the conversion of DOPA to melanin; thus, melanin production is inhibited. It is also thought to inhibit the synthesis of RNA
and DNA leading to the destruction of melanocytes. Its effectiveness is increased when used in combination with other drugs as mentioned above.

2. **Tretinoin is commonly used as an over-the-counter lightening agent** in the treatment of melasma.

3. ![Image: "A one gram vial of TXA." by James Heilman, MD. License: CC BY-SA 4.0](image)

**Tranexamic acid is mainly an antifibrinolytic** but is used in the treatment of melasma as it also causes inhibition of plasmin activity induced by ultraviolet rays in keratinocytes. It indirectly inhibits melanogenesis. It can be used by oral, topical or intradermal route in the treatment of melasma. A micro-injection is used for the intradermal route. The prescribed dosage for the drug is 250 mg two times a day orally and 4 mg/ml weekly for 12 weeks intradermally. This drug has minimal side effects and a good safety profile.

4. **n-Butylresorcinol is basically a resorcinol derivative** which causes inhibition of enzymes involved in melanin biosynthesis, inhibition of tyrosinase, as well as the tyrosinase-related proteins. Although the drug is not yet being widely used, it has shown promising results and minimum side effects.

5. **Oligopeptides are the newer drugs** which mainly inhibit the tyrosinase enzyme.

6. **Botanical extracts** are also being used with good success rate these days. They include the grape seed extract, orchid extract, aloe vera extract, pycnogenol, marine algae extract, cinnamic acid, flavonoids, mulberry extracts, green tea extracts, coffeeberry, soy, licorice extract, umbelliferone, and Boswellia. They are mainly used for their antioxidant effect.

### Chemical peels

Various chemical peels are **used as an adjunct to medicinal treatment**. They comprise of **tretinoin peel, obagi blue peel, as well as a glycolic acid peel**.

Chemical peels can lead to short-term improvement if the pigmentation is epidermal. On the application of peels, the skin initially turns red and then black. The black eschar peels off within a week. However, in some cases, post-inflammatory hyperpigmentation is a complication.

1. **Tretinoin peel** is being used in view of its effectiveness as cream. Tretinoin peeling helps in the lightening of the pigmentation in melasma. It can also be used as a peeling mask. It does not have any side-effects and has good patient compliance.

2. **Obagi blue peel** is made up of a predetermined concentration of trichloroacetic acid and a blue peel base. The blue peel base is composed of glycerine and amino
fruit acid peels.

Laser therapy and dermabrasion

Different lasers are being used for the treatment of melasma. They are as follows:

1. **Green light**: Flashlamp-pumped PDL (510 nm), frequency-doubled Q-switched neodymium: Yttrium aluminum garnet-532 nm (QS Nd: YAG)
2. **Red light**: Q-switched ruby (694 nm), Q-switched alexandrite (755 nm)
3. **Near-infrared**: QS Nd: YAG (1064 nm)

For melasma, QS Nd:YAG (neodymium-doped yttrium aluminum garnet: Nd:Y<sub>3</sub>Al<sub>5</sub>O<sub>12</sub>) is the most commonly used laser treatment. The combination of ablative and pigment selective lasers has also been used. Ablative lasers remove the epidermis containing excess melanin which is then followed by the use of Q-switched pigment selective laser that can target the dermal melanophages. Lasers should be preferred only in cases of refractory melasma.

Prevention of Melasma

Individuals should avoid sun exposure as much as possible. Sun exposure is an important etiologic factor, thus avoidance of sun exposure and use of broad-spectrum sunscreen lotions containing zinc oxide or titanium dioxide are of paramount importance for effective clinical management as they provide protection from both UVA, as well as UVB.

Various sun protection accessories, such as wide-brimmed hats, must be used meticulously. Also, harsh cosmetic products and waxing of facial hair should be avoided. Use of oral contraceptives with a high estrogen content should be avoided.

Conclusion

Melasma has a multi-factorial etiology and thus its treatment is challenging. Proper identification of the etiologic factors helps in the development of an accurate treatment plan and lower recurrence rate. A wide range of treatment options is presently available which helps in providing treatment that is more efficacious, having lesser side effects and longer periods of remission.

More randomized controlled trials are necessary for evaluation of the efficacy of newer compounds. For maximal favorable results and prevention of relapse, ideal combination therapies must be designed and studied.
References


Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our legal information page.