Oral pigmentation
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Abstract
Change in color of oral mucosa reflects the underlying health status, which is either local or systemic. This color change is due to pigmentation, which may be physiological or pathological. Pigmentation in pathological conditions range from localized anomalies of to potentially life-threatening conditions. Since the dental professionals encounter a number of pigmented lesions in the oral cavity, it is important to have a comprehensive knowledge about their etiology, clinical manifestations, and their management. In the following review various pigmentations of the oral cavity are discussed.

Keywords
Endogenous pigmentation, exogenous pigmentation, melanogenesis, melanin, oral pigmentation

Introduction
The pigmentation in oral cavity may be caused by the accumulation of one or more pigments which further leads to change in color of the tissues. There are several degrees of chromatic variegation observed in both physiological and pathological conditions. The normal color of healthy tissues of oral mucosa is pale pink, but there is change in color from pink to red due to inflammation. This coloration is caused by number of factors, one of which is pigmentation.

Classification of Oral Pigmentation
Oral pigmentation has been associated with variety of lesions and conditions. Differential diagnosis of oral pigmentation is made according to the following situations as shown in Table 1.

Endogenous pigmentation
Endogenous pigmentations of the oral mucosa are produced by the body’s own metabolism. These include melanin, hemoglobin, and hemosiderin. The most important of them is melanin, which is synthesized by melanocytes in the basal epithelial layer and then transferred to keratinocytes.

Physiology of melanin pigmentation
There is more occurrence of melanin pigmentation in the oral cavity of darker skinned individual’s than light-skinned individual’s. The coloration is produced by melanocytes that contain melanin in basal cell layer of epithelium. It produces melanin in membrane-bound organelles called as melanosomes. The hematoxylin and eosin stained section shows average number of melanocytes as 1 of 10 cells in the basal layer of epithelium.

Melanogenesis
Melanin is a pigment produced by melanocytes that reside in the basal layer of the epidermis. It is stored in vesicles called melanosomes and is transferred to adjacent epithelial cells via dendritic processes. Melanin protects DNA from the ionizing, damaging effect of ultraviolet radiation. It is the end-product of complex multistep transformations of L-tyrosine, are polymorphous and multifunctional biopolymers, represented by:
- Eumelanin
- Pheomelanin
- Neuromelanin and
- Mixed melanin pigment.
According to this theory melanin is present in specialized pigment producing cells called as melanocytes, which got transferred in granular form into neighboring epidermal cells. Masson has been vindicated and his “cytocrine” theory is widely accepted.

Birbeck and his associates (1956) found melanocytes exhibited a cell. When the sagittal section of hair follicle was done at different levels, it revealed that portion of cytoplasmic process of the hair melanocyte appeared as phagocytized by cortical cell. Later, the cell wall got disappeared and melanin granules got dispersed throughout in cytoplasm of cortical cells.[10]

### Endogenous Pigmentation (Melanin)

#### Oral melanotic macule

The term melanotic macule has been used to describe a benign pigmented lesion of the oral cavity.[11] It represents an increase in synthesis of melanin pigments by basal cell layer melanocytes without increase in number of melanocytes. It is attributed to actinic exposure and therefore occurs on vermilion border of the lower lip. It is brown or brown black pigmentation, <1 cm in diameter and constant in size. It is asymptomatic condition.[12] There is no need of further treatment once diagnosis got established [Figure 2].[13]

#### Nevus

“Nevus” (Latin, “birthmark”), refers to the pigmented lesion composed of nevus cells. The nevus cells are derived from pigment cells that migrate from the neural crest to the epithelium. They are present as flat, slightly raised lesions or even as a tumor.[14,15] The color of nevus can be bluish-gray, brown or almost black and occasionally they can be non-pigmented.[16] About 80% of oral nevi may be smaller than 1 cm in the greatest diameter.[14] Surgical excision of all intraoral pigmented nevi is recommended.[17]

#### Malignant melanoma

Melanoma is a neoplasm of epidermal melanocytes.[17] They are rear neoplasm’s and accounts for <1% of all oral malignancies. They are commonly found on hard palate followed by the gingiva.[16] Its color varies from brown to black to blue.[3] In oral cavity, it appears on anterior labial gingiva and the anterior aspect of the palate as brown or black plaques with irregular outline.[12]

#### Basilar melanosis with incontinence

Pigmentation of oral mucosa as a direct consequence of smoking has received more emphasis in the literature. It is known excessive melanin pigmentation results from basilar melanosis.[18] Melanin stimulation may represent a protective mucosal response to either the heat of the smoke or to an irritant within the cigarette.[19] It is present on lateral tongue, buccal mucosa, palate etc.[3] The diagnosis can be made by biopsy of the lesion. It usually disappears within 3 years of smoking cessation.[15]
Endogenous Pigmentation (Hemoglobin)

**Varix**

A varix is a dilated, tortuous vein, most commonly a vein which is subjected to increased hydrostatic pressure but poorly supported by surrounding tissue. This type of pigmentation mainly found on ventral surface of the tongue. It appears as multiple bluish purple, irregular, soft elevations. If thrombus is present than it does not blanch on pressure. It is usually small in diameter ranging from 2 to 4 mm. The lesion can be excised or removed by electrosurgery or cryosurgery.

**Hemangioma**

Hemangioma is a proliferation of endothelial cells of vascular channels. It may be congenital and traumatic in origin. The cause is unknown but one of the reasons suggested is role of estrogen signaling in hemangioma proliferation. They are rare in the oral cavity but may occur on tongue, lips, buccal mucosa, gingiva, palatal mucosa, salivary glands, alveolar ridge, and jaw bones. It may appear as a flat reddish blue macule (port-wine stain) to a nodular blue tumefaction. The range of treatment includes surgery, flash lamp pulsed laser, intralesional injection of fibrosing agent and electrocoagulation.

**Kaposi sarcoma**

It is a multicentric proliferation of vascular and spindle cell components. This tumor is incriminated with HIV/AIDS. Immunosuppression is highly associated with Kaposi’s sarcoma. Oral lesions occur on the posterior hard palate, gingiva, and tongue. In rare cases the patient has a single cutaneous lesion, often on the head or neck. It begins as a flat red macule of variable size and irregular configuration. Nodular lesions may become unsightly and interfere with mastication; in this situation, therapy may be desirable and includes electrocautery, excision. For AIDS associated Kaposi sarcoma highly active anti-retroviral therapy is useful for managing the condition.

**Hereditary hemorrhagic telangectasia**

It is also known as Osler Weber Randu syndrome. Papules are red or brown rather than purple. The lesions blanch upon pressure and regain their original color upon release. It is characterized by multiple, round or oval papules measuring <0.5 cm in diameter. The early oral lesion is a cherry-red macule ranging from 1 to 3 mm in diameter. It occurs in
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a number of conditions like ataxia-telangiectasia, pregnancy, chronic liver disease. The treatment modality for telengectatic areas to be removed is by electrocautery under local anesthesia.

Angiosarcoma

Angiosarcoma is a malignant mesenchymal tumor with a differentiation into vascular endothelium. It is also known as malignant hemangioendothelioma, angioblastoma, hemangiosarcoma, and intravascular endothelioma. In general, angiosarcoma is a very aggressive tumor. In oral cavity involves lips, tongue, and floor of mouth, cheek and palate. It appears as a poorly demarcated nodular tumor that is red-blue to purplish in color. There is no gender predilection. Surgery remains the mainstay of therapy. A combined modality of treatment using post-operative radiotherapy may be used.

Endogenous Pigmentation (Hemosiderin)

Ecchymosis

Ecchymosis commonly known as bruises, frequently occur after injury. Traumatic ecchymosis is common on the lips. Whenever trauma occurs, the erythrocytes comes out in to submucosa and appear as a bright red macules and then lesion become brown in color in few days, as hemoglobin is degraded into hemosiderin. They are larger than pin point spots and are larger than petechiae (1-3 mm). The application of ice or use of epinephrine employed to prevent ecchymosis formation.

Petechiae

Petechiae are submucous or subcutaneous minute pinpoint hemorrhages. Capillary hemorrhages will appear red initially and turn brown in a few days once the extravasated red cells have lysed and have been degraded to hemosiderin. In most cases, the petechiae are identified on the soft palate, although any mucosal site may be affected. Surgery should not be performed until the defect has been identified and treated.

Hemochromatosis

Hemochromatosis is a chronic, progressive disease that is characterized by excessive iron deposition in the liver and other organs and tissue, leading to organ toxicity. It is also called as bronze diabetes. The cause for hemochromatosis is a genetic defect, which leads to excessive iron absorption. The palate and gingiva are most commonly affected in oral cavity. The oral pigmentation is often diffuse and brown to gray in appearance. It is treated by phlebotomy.

Exogenous pigmentation

Exogenous pigments are usually traumatically deposited directly into the submucosa. However, some may be ingested, absorbed, and distributed hematogenously, to be precipitated in connective tissues, particularly in areas subject to chronic inflammation, like gingiva.

Amalgam tattoo

The single most common type of focal pigmentation in the oral mucosa is the amalgam tattoo. They are found in large amalgam restorations. The most common sites are on gingiva and alveolar mucosa with mandibular region being affected more commonly than maxillary region. Pigmentation is blue black in color. If there is no radiographic evidence of amalgam, the lesion is not in proximity to any restored tooth, or the lesion suddenly appears, a biopsy is necessary.

Graphite tattoo

Pencil points are occasionally broken off in gingival tissue and if not completely removed, may cause permanent discoloration as graphite tattoo. The color of the lesion can be gray or black. Both melanoma and graphite tattoo commonly occurs on palate so it’s mandatory to differentiate them from each other. Graphite particles resemble those of amalgam.

Hairy tongue

Hair tongue is a defective desquamation of the filliform papillae. It involves the dorsum of tongue, particularly the middle and posterior one-third. In hairy tongue the length of filiform papillae can be more than 15 mm. Its color can be brown, white or green depending on the specific etiology. The filiform papillae can get removed by simply brushing the tongue with a toothbrush.

Pigmentation Related to Heavy Metal Ingestion

Different types of heavy metal pigmentations are as following:

- Bismuthism
- Plumbism
- Mercurialism
- Argyriosis
- Arsenism
- Auric stomatitis.

Figure 3: Hairy tongue
Bismuthism
It is due to bismuth poisoning caused by medicinal use of bismuth containing preparation. This pigment is produced by the action of hydrogen sulfide on the bismuth compound. Patients often complain of a metallic taste with burning sensation in the oral cavity. Large, extremely painful, shallow ulcerations are seen at times on the cheek mucosa in molar region. "Blue black" bismuth line appears to be well demarcated on gingival papillae. Establishing and maintaining oral hygiene and stoppage of use of bismuth will decrease its effect.

Plumbism
It is caused by lead in the paints, glazes, cooking vessels, batteries, ointment and containers. Oral tissues are exposed to lead through direct contact with ingested lead and through secretion of lead in the saliva. There is a metallic taste which is accompanied by excessive salivation and dysphagia. When exposure to lead is very high and oral hygiene is very poor, a line known as “burtonian line” is seen which is present along the gingival margin. Lead can be removed from the body by using chelating agents.

Mercurialism
It may be chronic or acute. It is also called pink disease or acrodynia. It is an uncommon disease caused due to a mercurial toxicity reaction, either actual mercury poisoning or, more likely, an idiosyncrasy to the metal. Patient will exhibit profuse salivation. Mastication is difficult due to pain. The gums are of a deeper hue than normal. Atropine or belladonna can be prescribed to lessen the salivary flow.

Argyriosis
It is also called as argyrosis which occurs due to chronic exposure to silver compound. The exposed body surfaces, including the nail beds are deeply discolored. The skin is slate gray, violet or cyanotic and in marked cases, there is even suggestion of metallic luster. Pigmentation is distributed diffusely throughout the gingival and mucosal tissue. The source of contact should be eliminated.

Arsenism
It occurs due to arsenic poisoning from industrial exposure or intentional use or due to therapeutic consumption. Oral tissues are extremely painful, become intensely inflamed and severe gingivitis may develop. The mouth is dry. Tissues are deep red in color. Local contact with arsenic trioxide often produces ulceration. Surface anesthetic ointment or rinses such as lidocaine or dylonine solution should be prescribed.

Auric stomatitis
Gold is useful for the treatment of rhesus arthritis, lupus erythematosus and leprosy. Vesiculations and ulcerations of the oral mucosa occur due to its excess. It is the most common complaint of the patient who is receiving gold therapy. It leads to faint blue or purple discoloration. Discontinuation of gold therapy and alkaline mouthwashes will decrease its effect.\textsuperscript{[12]}

Idiopathic pigmentation
A solitary pigmented lesion may cause more suspicion; one of them is Laugier–Hunziker syndrome. The pathogenesis of this lesion is increased melanosomes and its migration to basal cell layer of epithelium.\textsuperscript{[10]} This condition more commonly develops in Caucasian or light-skinned individuals. It is characterized by asymptomatic, lenticular and \(<5\text{ mm}\) in diameter. This lesion is mostly seen on lips, hard palate and buccal mucosa. The use of laser and cryotherapy can be done for treatment of the lesion \([\text{Figure 4}].\textsuperscript{[4]}\)

Investigations
Various investigations required in diagnosis of oral pigmentation are as following:
- History
- Dermoscopy
- Binocular stereo microscope
- Pigmentation
- Biopsy.

History
The history includes full medical and dental history of patient with pigmented lesion. Than extraoral and intraoral examinations and laboratory tests should be performed. The history related to pigmented lesion includes presence of systemic signs and symptoms, onset and duration of the lesion, presence of associated hyperpigmentation.\textsuperscript{[13]}

Dermoscopy
Dermoscopy is a non-invasive diagnostic technique, which is used for the examination of pigmented lesions and early detection of malignancy. It provides non-invasive, magnified visualization of the pigmented lesions and helps in differentiating the lesions from other benign or malignant conditions.
of cutaneous melanoma. It also helps to avoid unnecessary excisional biopsies and extensive surgeries of oral cavity. [30]

**Binocular stereo microscope**

This diagnostic technique has been shown to be effective in discriminating melanocytic from non-melanocytic lesions and benign versus malignant melanocytic processes. [4]

**Pigmentations**

Abnormal insoluble deposits, yellow, brown or black without staining, and not distinctively stained with H and E, are frequently encountered. Pigments play an important part in the diagnosis of diseases. Pigments are identified either by their color, size and shape or by chemical testing. [40]

**Biopsy**

Oral biopsy is considered essential for proper and definitive diagnosis of diseases of the oral mucosa, and for planning of appropriate treatment for the disease. [23,41]

**Conclusion**

The variation from the normal color of oral tissues should always attract one’s attention, as a proportion of these changes may indicate potential underlying pathology. As the diagnosis of pigmented lesions in oral cavity and perioral tissues is difficult, even epidemiology may be of some help in orienting clinicians. The definitive diagnosis usually requires biopsy and histopathologic examination of the lesion. Thus, an understanding of various disorders and substances that can contribute to oral and perioral pigmentation is essential for appropriate evaluation, diagnosis, and management of patient.

**References**
