PRECANCEROUS LESIONS IN ORAL CAVITY

Assoc.Prof. G. Tomov, PhD

Oral Pathology Division
Faculty of Dental Medicine - Plovdiv
Introduction

- Oral cancer constitutes an important entity in the field of Oral and Maxillofacial surgery

- The global incidence of oral cancer is 500,000 cases per year with mortality of 270,000 cases

- Some oral cancers initiate as a De Novo lesion while some are preceded by Oral premalignant lesions and conditions
Introduction

- Various premalignant lesions, particularly red lesions and some white lesions have a potential for malignant change.
- Practitioners will see many oral white lesions but few carcinomas. However they must be able to recognize lesions at particular risk and several features which help to assess the likelihood of malignant transformation.
- The accuracy of such predictions about premalignant lesions and conditions is low but the process of identifying “at risk” lesions is fundamental for diagnosis and treatment planning.
The terms premalignant (pre- preliminary and malignant-cancerous) lesions and conditions were coined by Romanian physician Victor Babeş in 1875.
Premalignant condition is defined as by WHO workshop 2005: ”It is a group of disorders of varying etiologies characterized by mutagen associated, spontaneous or hereditary alterations or mutations in the genetic material of oral epithelial cells with or without clinical and histomorphological alterations that may lead to oral squamous cell carcinoma transformation”

(Ref: Oral potentially malignant disorders: Précising the definition) - Oral Oncology journal (2012)
### Premalignant lesions
- Leukoplakia
- Erythroplasia
- Leukokeratosis nicotina palatinae
- Candidiasis
- Carcinoma in situ

### Premalignant conditions
- Oral lichen planus
- Actinic keratosis
- Syphilis
- Discoid lupus erythematosus
- Sideropenic dysphagia
**Group I:** Morphologically altered tissue in which external factor is responsible for the etiology and malignant transformation.

**Group II:** Morphologically altered tissue in which chronic inflammation is responsible for malignant transformation (chronic inflammation mediated carcinogenesis).

**Group III:** Inherited disorders that do not necessarily alter the clinical appearance of local tissue but are associated with a greater than normal risk of PMD or malignant transformation.

**Group IV:** No clinically evident lesion but oral cavity is susceptible to Oral squamous cell carcinoma.
Group I: Morphologically altered tissue in which external factor is responsible for the etiology and malignant transformation

Group I

1. Habit related:

   a. Tobacco associated lesions • Leukoplakia • Tobacco pouch keratosis • Stomatitis palatine nicotini
   b. Betel nut associated • Oral submucous fibrosis c. Sanguinaria-associated keratosis

2. Non-habit related:

   • Actinic cheilosis

   • Chronic candidiasis (Certain strains of Candida have been shown to produce nitrosamines a chemical carcinogen (external factor) and hence, candidiasis is included under Group I.)
Group II: Morphologically altered tissue in which chronic inflammation is responsible for malignant transformation (chronic inflammation mediated carcinogenesis).

Group II

a. Chronic inflammation caused by internal derangement.
   1. Lichen planus
   2. Discoid lupus erythematosus

b: Chronic inflammation caused by external factors.
   1. Chronic mucosal trauma
   2. Lichenoid reactions
   3. Poor oral hygiene
   4. Chronic infections • Chronic bacterial infections • Chronic viral infections • Chronic fungal infections
   5. Other pathologies associated with prolonged untreated chronic inflammation of the oral cavity.
Group III

Inherited disorders that do not necessarily alter the clinical appearance of local tissue but are associated with a greater than normal risk of PMD or malignant transformation. 

1. Inherited cancer syndromes
   • Xeroderma pigmentosum
   • Ataxia telangiectasia
   • Fanconi’s anemia
   • Li Fraumeni syndrome

2. Dyskeratosis congenita
3. Epidermolysis bullosa
4. White sponge nevus
5. Darier’s disease
6. Hailey–Hailey disease
Group IV: No clinically evident lesion but oral cavity is susceptible to Oral squamous cell carcinoma

Group IV

1. **Immunosupression**
   * AIDS
   * Immunosupression therapy (for malignancy or organ transplant)

2. **Alcohol consumption and abuse**

3. **Nutritional deficiency**
   * Sideropenic dysphagia
   * Deficiency of micronutrients
Leukoplakia

- Oral leukoplakia, as defined by the WHO, is “A predominantly white lesion of the oral mucosa that cannot be characterised as any other definable lesion.” (Ref – WHO workshop 2012) J Oral Pathol Med (2012) 36: 575–80
The exact etiology is unknown. But some predisposing factors can be identified. PREDISPOSING FACTORS ARE BEST REMEMBERED AS 6 S

- Smoking
- Spirit
- Sharp tooth
- Spicy food
- Syphilis
- Sepsis
Etiology

- **Tobacco.** Most important causative factor. Pindborg & colleagues pointed out that tobacco produces a specific effect on the oral mucosa, leading to a characteristic appearance of pumice stone.

- **Alcohol.** Heavy consumption of alcohol is second most important risk factor, it acts synergistically with tobacco.

- **Candida infection.** Candida albicans infection (chronic hyperplastic candidiasis) may play a role in the etiology of leukoplakia.

- **Human papilloma viruses.**

- **Vitamin Deficiency.** Vit A deficiency will cause metaplasia and keratinization of epithelial structures (particularly glands).
N.B. Stomatitis palatine nicotini
Candidial leukoplakia
Histopathology of candidial leukoplakia
Clinical features

- Male predilection. Most common in 40 – 60 years of age (Recent studies show higher incidences in young adults). It occurs on the lateral margins of the tongue often bilaterally. The lesions are white, sometimes corrugated and may be proliferative to produce a shaggy carpet like appearance

- Hairy leukoplakia is associated with Epstein-Barr virus (EBV) and occurs primarily in HIV-positive individuals.
• Leukoplakia is purely a clinical terminology and histopathologically it is reported as epithelial dysplasia.
• WHO in 2005 proposed five grades of epithelial dysplasia based on architectural disturbances and cytological atypia.
• Leukoplakia means “white plaque” (from Greek)
• The term is strictly a clinical one and does not imply a specific histopathologic tissue alteration.
• It makes the diagnosis dependent not so much on definable appearances but on the exclusion of other entities that appear as oral white lesions.
A clinical staging system for oral leukoplakia (OL-system) on the lines of TNM staging was recommended by WHO in 2005 taking the size (L) and the histopathological features (P) of the lesion into consideration.

Clinical Staging

- **Lx**: Size not specified.
- **L1**: Single or multiple lesions together <2 cm.
- **L2**: Single or multiple lesions together 2-4 cm.
- **L3**: Single or multiple lesions together >4 cm.
- **Px**: Epithelial dysplasia not specified. • P0: No epithelial dysplasia.
  • P1: Mild to moderate epithelial dysplasia.
  • P2: Severe epithelial dysplasia.

**Stage I**: L1 P0.  **Stage II**: L2 P0.  **Stage III**: L3 P0 or L1/ L2 P1.  **Stage IV**: L3 P1 or Lx P2.
N.B. Leukoplakia is purely a clinical terminology and histopathologically it is reported as epithelial dysplasia.

WHO in 2005 proposed five grades of epithelial dysplasia based on architectural disturbances and cytological atypia:

1. Squamous Hyperplasia
2. Mild Dysplasia – better prognosis
3. Moderate Dysplasia
4. Severe Dysplasia

It has been recently proposed to modify the above 5-tier system into a binary system of ‘high risk’ and ‘low risk’ lesions to improve clinical management of these lesions.
Hyperplasia → Mild dysplasia → Moderate dysplasia → Severe Dysplasia/CIS → Invasive SCC

Low-grade dysplasia
Generally low cancer risk

High-grade dysplasia
Generally high cancer risk
Carcinoma in situ
Clinical Types:
1. Homogenous 2. Non-homogenous

HOMOGENOUS
Uniform white patch lesion with smooth or corrugated surface sometimes, slightly raised mucosa. Usually plaque like, some are smooth, may be wrinkled or criss-crossed by small crack or fissure.

Malignant transformation – 1 to 7%.


NON-HOMOGENOUS LEUKOPLAKIA TYPES
1. Ulcerative or Erosive
2. Verrucous (proliferative verrucous leukoplakia) or Nodular
3. Speckled (High malignant transformation)

(Ref- WHO workshop 1994)
NON-HOMOGENOUS LEUKOPLAKIA TYPES

1. **Ulcerative.** Red ulcerative lesion (Atrophic epithelium) with small white specks or nodules over it.

2. **Verrucous.** Warty surface (white lesion with hyperplastic surface) or heaping up of the surface or like a nodule on an erythematous background. White lesion with a granular surface is associated with candida.

3. **Speckled.** Mixed red and white patches on an irregular surface.
EVOLUTION!!!
• Male predilection
• Mostly occurs in 4th to 7th decade of life.
• Oral leukoplakias are found on the upper and lower alveolus (36%) buccal mucosa (22 %), lips (11%), palate (11%), floor of mouth (9%), gingiva(8%), Tongue(7%), retromolar trigon (6%)

(Ref - Oral potentially malignant disorders: Precising the definition) Otorhinolaryngology clinics – An International journal may-sept. 2009
A **provisional diagnosis** of leukoplakia is made when a predominantly **white lesion** at clinical examination cannot be clearly diagnosed as any other disease or disorder of the oral mucosa.

A **biopsy is mandatory**. A definitive diagnosis is made when any aetiological cause other than tobacco use has been excluded and histopathology has not confirmed any other specific disorder.
Differential diagnosis

- White sponge nevus
- Acute pseudomembranous candidiasis
- Leukoedema
- Lichen planus (plaque type)
- Morsicatio buccarum
White sponge nevus (Cannon's disease) is an autosomal dominant condition of the oral mucosa. It is caused by mutations in certain genes coding for keratin 4 or 13, localized in 12q13 and 17q21-q22 chromosomes which causes a defect in the normal process of keratinization of the mucosa. This results in lesions which are thick, white and velvety on the inside of the cheeks within the mouth. Usually, these lesions are present from birth or develop during childhood. The condition is entirely harmless, and no treatment is required.
Leukoedema is a blue, grey or white appearance of mucosae, particularly the buccal mucosa. It is a harmless and very common condition. Because it is so common, it has been argued that it may in fact represent a variation of the normal appearance rather than a disease, but empirical evidence suggests that leukoedema is an acquired condition caused by local irritation. It is found more commonly in black skinned people and in those who smoke.
Lichen planus
Morsicatio buccarum
Treatment

The first step in treatment is to arrive at a definitive histopathologic diagnosis. Therefore, a biopsy is mandatory and will guide the course of treatment. Tissue to be obtained for biopsy, should be taken from the clinically most "severe" areas of involvement. • Multiple biopsies of large or multiple lesions may be required.
Incisional biopsy
Diagnosis: Leukoplakia without dysplasia
• Photodynamic Therapy
• L-Ascorbic Acid (Vitamin C)
• α-Tocoferol (Vitamin E)
• Retinoic Acid (Vitamin A)
• Vitamin A derivative, isotretinoin, and 13-cis retinoic acid: 28,500 IU per day.
• Beta-carotene 150,000 IU of beta-carotene twice per week for six months.
• Bleomycin-Topical bleomycin in treatment of oral leukoplakia was used in dosages of 0.5%/day for 12 to 15 days or 1%/day for 14 days.
Isotretinoin (13-cis-retinoic acid, a form of vitamin A) - alone or in combination with beta-carotene has been reported to reduce or eliminate some leukoplakic lesions in short term studies.

N.B. However, to date there is insufficient evidence from well-designed clinical trials to support the effectiveness of such medical therapies in treating oral dysplasia or preventing the progression of oral dysplasia to squamous cell carcinoma.
FOUR methods are available for the removal of leukoplakia patches of the oral mucosa:

1. Scalpel excision / Stripping
2. Electrocautery
3. Cryotherapy
4. CO2 or Er:YAG Laser therapy
Surgical Management - Scalpel Excision

Traditional method. The area is outlined including few millimeters of normal tissue. It is incised with scalpel and patch (leukoplakia) is undermined by scalpel or by blunt dissection to a depth of 2 to 4 mm. This allows leukoplakia to be removed in one piece. The mucosal defect if small is closed primarily or it is covered by transported local mucosal flaps. Larger defects are grafted with split thickness skin graft.

• Advantages – whole of patch can be taken in one piece for histopathological examination and in addition no special equipments are required.

• Disadvantages - Persistent bleeding, which makes accurate excision difficult. In the floor of mouth care has to be taken for submandibular duct and lingual artery. There is contraction and scarring resulting in restricted movement of oral soft tissues. The skin grafts when used remains white and masks any recurrence of leukoplakia. Recurrence rate - 20 to 35 %
Electrocautery (Fulguration). This procedure requires local or general anaesthesia. The healing process is slow and painful. Multiple areas of the lesion are pierced with electrocautery and left to heal.

Cryotherapy is a method of superfreezing tissue in order to destroy it. Cryotherapy is done using a cotton swab that has been dipped into liquid nitrogen or a probe that has liquid nitrogen flowing through it. The technique involves freezing the mucosa with the cryoprobe for 1.5 to 2 minutes, then waiting for 2 minutes, followed by further freezing of 1.5 to 2 minutes. Thicker lesions may require 2 to 3 minutes freezing.
Advantages

1. Simple, Painless, out-patient procedure, well tolerated by patients including the elderly.
2. During the healing phase there is absence of infection and pain and the wound is cleaner without foul odour.
3. General anaesthesia is not required.
4. There is little scar formation,
5. There is no intra or post operative bleeding and the procedure may be repeated on several occasions.

Disadvantages

1. There is no surgical specimen for histopathological examination!!!! (N.B.)
2. The zone of tissue elimination is variable resulting in inaccurate margin of destruction. Post-operatively there is marked oedema.
3. There is unpleasant delayed necrosis of the treated area which separates as a slough and it might stimulate epithelial changes (particularly in cases of advanced stages of pre-malignant state).
CO2 and Er:YAG Laser Therapy. This destroys soft tissue in a unique manner and is ideal means of removing leukoplakia.

- CO2 laser beam wavelength – 1060nm, Er:YAG laser beam wavelength – 2940nm
- Well absorbed by water and hence by soft tissues.
- The absorbed energy causes vaporisation of the intra and extra cellular fluid and destruction of cell membrane. The cell debris are released and burned in the laser beam, depositing a carbonised layer on the tissue surfaces.
- There are two techniques which are used to remove the leukoplakia using CO2 or Er:YAG laser – Excision and Vaporization
To excise a patch of leukoplakia, the laser is used to cut around the margins, which can be held in tissue forceps while the laser undermines the leukoplakic patch.

Vaporization of leukoplakia is by moving the laser beam back and forward across the surface of lesion. It has the risk of leaving small bits of abnormal tissue which are deep under thickly keratinized tissue.
Advantages:
1. There is excellent visibility and precision when dissecting through the tissue planes
2. There is little contraction or scarring
3. Patients usually feel less pain when compared with scalpel excision

Disadvantages:
1. High cost of equipment
2. Requires protection of patient’s as well as surgeon’s eye
3. There is delayed wound healing. 4. Frame and colleague reported a 20 % recurrence rate following removal of leukoplakia by CO2 laser therapy
Laser ablation with Er:YAG laser
After 3 months
Erythroplakia (erythroplasia of Queyrat)

- This was first described by Louis Queyrat in 1911

- WHO definition: A fiery red patch that cannot be characterized clinically or pathologically as any other definable disease
Erythroplakia (erythroplasia of Queyrat)

- **Etiology** - Unknown
  - Contributing factors include tobacco use, alcohol consumption

- **Incidence** - It is more common in males and occurs more frequently in the 6th and 7th decade of life

- **Clinical Presentation** - Red, often velvety, well-defined patches. Most commonly present on floor of mouth, retromolar trigone area, lateral tongue
  - Usually asymptomatic
  - May be smooth to nodular
Erythroplakia (erythroplasia of Queyrat)

- **Homogenous form** which appears as a bright red, soft velvety lesion with straight or scalloped well demarcated margins, often quite extensive in size, commonly found on the buccal mucosa and sometimes on the soft palate, more rarely on the tongue and floor of the mouth.

- **Speckled leukoplakia / erythroplakia** which is soft, red lesions that are slightly elevated with an irregular outline and a granular or fine nodular surface speckled with tiny white plaques.
Erythroplakia (erythroplasia of Queyrat)

Diagnosis:
• Appearance
• History of tobacco/alcohol use
• Biopsy results

Differential Diagnosis: Erythematous (atrophic) candidiasis • Kaposi’s sarcoma • Ecchymosis • Contact stomatitis • Vascular malformation • Squamous cell carcinoma • Geographic tongue/erythema migrans

Treatment. The treatment is same as that for invasive carcinoma or carcinoma-in-situ like surgery, radiation and cauterisation.
Lichen planus

- Lichen Planus Etiology – Unknown

- Autoimmune. T cell–mediated disease targeting basal keratinocytes

- Lichenoid changes associated with galvanism, graft-versus-host disease (GVHD), certain drugs, contact allergens
Lichen planus – presentation and clinical forms

Bilateral and often symmetric distribution

Oral site frequency: **buccal mucosa** (most frequent), then **tongue, gingiva, lips** (least frequent)

Variants (**erosive and non-erosive**):

- Reticular (most common oral form)
- Papular
- Plaque like
- Atrophic
- Erosive (painful) – considered precancerous lesion
- Bullous (rare) – considered precancerous lesion
Reticular form of OLP (most common oral form)
Reticular form of OLP (skin lesions)
Plaque like form of OLP (rare)
Desquamative gingivitis
- atrophic form of oral lichen planus
Erosive form of oral Lichen planus
Bullous form of oral lichen planus
Lichen planus – Diagnosis, D.D. and treatment

Diagnosis

• Examination of oral mucosa and skin
• Biopsy
• Direct immunofluorescence (helps confirm diagnosis)

Differential Diagnosis • Lichenoid drug eruptions • Erythema multiforme • Lupus erythematosus • Contact stomatitis • Mucous membrane pemphigoid

Treatment of Oral Lichen Planus:
• Mild to moderate: topical corticosteroids, laser ablation
• Severe: systemic immunosuppression, chiefly prednisone, topical tacrolimus ointment
Clinical case of reticular OLP
Histological confirmation: Lichen planus
Laser ablation with Er:YAG laser
Before treatment

6 months after treatment
Lichen planus
Photodynamic therapy
Actinic keratosis is also potentially malignant disorder associated with long term exposure to sun radiation and may be found on the vermilion border of the lips as well as other exposed skin surfaces.

Clinical features - On the skin surfaces and the vermilion border of the lip, the lesion is crusted and keratotic.

On the labial mucosa exposed to sun, a white area of atrophic epithelium develops with underlying scarring of the lamina propria.

When this atrophic tissue abrades or ulcerates, it is called actinic cheilitis.
When this atrophic tissue abrades or ulcerates, it is called actinic cheilitis.
Treatment: 5-flurouracil is found to be effective. But dysplastic changes in epithelium remain. So adequate follow-up is required unless surgical removal is done.

Source: „Red and white lesions of the oral mucosa“
INTRA EPITHELIAL CARCINOMA

- This occurs frequently on the skin (Bowen’s disease) but also on mucous membrane.

- Incidence - Shafer also found the occurrence as 23% in floor of the mouth, 22% on the tongue, 20% on the lip.

- It is more common in elderly men.

- 45% of the lesions of carcinoma in situ were leukoplakic, 46% were erythroplakic, 9% were a combination of leukoplakic and erythroplakic patches, 13% were ulcerated lesions, 5% were white ulcerated lesions, 1% were red ulcerated lesions and 11% didn’t have specific appearance.

TREATMENT: The lesions must be radically surgically excised
Cornu cutaneum
The lesion at the base of the keratin mound is benign in the majority of cases. Malignancy is present in up to 20% of cases, with squamous cell carcinoma being the most common type.
Pigmented lesions

Diffuse and bilateral

- Early onset
  - Physiologic pigmentation
  - Peutz-Jeghers syndrome
- Predominantly adult onset
  - With systemic signs and symptoms
    - Addison's disease
    - Heavy metal pigmentation
    - Kaposi's sarcoma
  - No systemic signs and symptoms
    - Drug-induced pigmentation
    - Postinflammatory pigmentation
    - Smoker's melanosis

Focal

- Red-blue-purple
  - Blanching
    - Hemangioma
    - Varix
  - Nonblanching
    - Thrombus
    - Hematoma
- Blue-grey
  - Amalgam tattoo
  - Other foreign-body tattoos
  - Blue nevus
- Brown
  - Melanotic macule
  - Pigmented nevus
  - Melanocanthoma
  - Melanoma

Source: Pigmented Lesions of the Oral Cavity: Review, Differential Diagnosis, and Case Presentations
Adel Kauzman, Marisa Pavone, Nick Blanas, Grace Bradley,
Normal pigmentation of the oral mucosa

Tyrosine $\rightarrow$ Dopa $\rightarrow$ Melanin

Tyrosinase

Melanocyte Stimulating Hormone
Intraoral brown and black lesions

- Normal
- Lentigo simplex
- Junctional activity
- Compound nevus
- Intramucosal
- Blue nevus
Mucosal Melanotic Macule

**Etiology**

- Most idiopathic, some postinflammatory, some drug-induced
- Multiple lesions suggest syndrome association, as follows:
  - Peutz-Jeghers syndrome
  - Laugier-Hunziker phenomenon
  - Carney’s syndrome
  - LEOPARD syndrome
Clinical Presentation

- Most in adulthood (fourth decade and beyond)
- Most are solitary and well circumscribed
- Lower lip vermilion border most common site, mostly in young women (labial melanotic macule)
- Buccal mucosa, palate, and attached gingiva also involved (mucosal melanotic macule)
- Usually brown, uniformly pigmented, round to ovoid shape with slightly irregular border
- Usually < 5 mm in diameter
Oral Melanotic Macule

Epithelium

Pigmented basal cell

Melanophages

Pigmented basal keratinocyte
**Microscopic Findings**

- Normal melanocyte density and morphology
- Increased melanin in basal cells and subjacent macrophages (mucosal melanotic macule)
- Increased melanin in basal cells with elongated rete pegs (ephelides)
Diagnosis

• Biopsy

Differential Diagnosis

• Melanoacanthoma
• Mucosal melanotic macule
• Congenital syndromes (Carney’s, Peutz-Jeghers, LEOPARD, Laugier-Hunziker)
Treatment

• Observation
• Biopsy for esthetics
• If increase in size or development of atypical signs occurs, macule should be removed to rule out malignant melanoma, particularly if on palate or alveolar mucosa.

Prognosis

• Excellent
Nevus

Etiology
• Unknown
• Lesion of melanocytic origin within mucosa and skin

Clinical Presentation
• Usually elevated, symmetric papule
• Pigmentation usually uniformly distributed
• Common on skin; unusual intraorally
• Palate and gingiva most often involved
Microscopic Findings

- Most are intramucosal ("dermal")
- Blue nevi are deeply situated and are composed of spindled nevus cells.
- Other variants are rare; junctional and compound nevi (no dysplastic nevi occur orally)
- Nevus cells are oval/round and are found in unencapsulated nests (theques).
- Melanin production is variable.
When nevus cells are located in the epithelium connective tissue junction, the lesion is called a *junctional nevus*. 
When nevus cells are located in connective tissue, the lesion is called an *intradermal nevus* or *intramucosal nevus*.
When nevus cells are located in a combination of zones, the lesion is called a compound nevus.
Intraoral

Cutaneous

Lamina propria

Intramucosal nevus

Junctional activity

Compound nevus
A fourth type of nevus, in which cells are spindle shaped and found deep in the connective tissue, is known as *blue nevus*. 
Diagnosis

• Clinical features
• Biopsy

Differential Diagnosis

• Melanoma
• Varix
• Amalgam tattoo/foreign body
• Mucosal melanotic macule
• Kaposi’s sarcoma
• Ecchymosis
• Melanoacanthoma
Treatment

• Excision of all pigmented oral lesions to rule out malignant melanoma is advised.
• Malignant transformation of oral nevi probably does not occur.

Prognosis

• Excellent
Nevus of Otta
Malignant Melanoma

Etiology

• Unknown

• Cutaneous malignant melanoma with relation to sun exposure or familial-dysplastic melanocytic lesions
Clinical Presentation

- Rare in oral cavity (< 1% of all melanomas) and sinonasal tract
- Most cases occur in those older than 30 years of age.
- Usually arises on maxillary gingiva and hard palate
- May exhibit early in situ phase: a macular, pigmented patch with irregular borders
- Progression to deeply pigmented, nodular quality with ulceration
- May arise de novo as a pigmented or amelanotic nodule
- Rarely may be metastatic to the oral cavity as a nodular, usually pigmented mass
Microscopic Findings

- Early stage: atypical melanocytes at epithelial–connective tissue interface, occasionally with intraepithelial spread
- Later infiltration into lamina propria and muscle
- Strict correlation to cutaneous malignant melanoma is not well established, although, as in skin, a similar horizontal or in situ growth phase often precedes the vertical invasive phase.
- Amelanotic forms may require use of immunohistochemical identification: S-100 protein, HMB-45, Melan-A expression
Early Changes of Melanoma

- Appear recently
- Change in degree of pigmentation
- Bleeding or ulceration
- Rapid growth (in size or elevated)
Melanoma malignum
Melanoma malignum
Melanoma malignum
Melanoma malignum
Diagnosis

- Biopsy
- High index of suspicion

Differential Diagnosis

- Mucosal nevus
- Extrinsic pigmentation
- Melanoacanthoma
- Kaposi’s sarcoma
- Vascular malformation
- Amalgam tattoo
- Mucosal melanotic macule
Melanoma
Immunohistochemical staining of HMB-45 (A) and S-100 (B) revealed diffuse positivity in the tumor cells.
Treatment

- Surgical excision
- Marginal parameters related to depth of invasion and presence of lateral growth
- Wide surgical margins; resection (including maxillectomy) for large, deeper lesions
- Neck dissection in cases of deep invasion (< 1.25 mm)

Prognosis

- Generally poor for most oral malignant melanomas
- Less than 20% survival at 5 years in most studies
Drug-Induced Melanosis

Etiology

• Occupational exposure—metals vapors (lead, mercury)
• Therapeutic—metal salt deposits (bismuth, cis-platinum, silver, gold); also nonmetal agents, such as chloroquine, minocycline, zidovudine, chlorpromazine, phenolphthalein, clofazimine, and others
Clinical Presentation

• Focal to diffuse areas of pigmentary change
• If heavy metals are the cause, a typical gray to black color is seen along the gingival margin or areas of inflammation.
• Palatal changes characteristic with antimalarial drugs and minocycline
• Most medications cause color alteration of buccal-labial mucosa and attached gingiva.
• Darkened alveolar bone with minocycline therapy (10% at 1 year, 20% at 4 years of therapy)
Diagnosis

• History of exposure to, or ingestion of, heavy metals or drugs
• Differentiation from melanocyte-related pigmentation by biopsy if necessary

Differential Diagnosis

• When localized: amalgam tattoo, mucosal melanotic macule, melanoacanthoma, mucosal nevus, ephelides, Kaposi’s sarcoma, purpura, malignant melanoma, ecchymosis
• When generalized: ethnic pigmentation, Addison’s disease
• If asymmetric, in situ melanoma must be ruled out by biopsy.
Treatment

• Investigation of cause and elimination if possible

Prognosis

• Excellent
Physiologic Pigmentation

Etiology
• Normal melanocyte activity

Clinical Presentation
• Seen in all ages
• Symmetric distribution over many sites, gingiva most commonly
• Surface architecture, texture unchanged
Racial pigmentation (melanoplakia)
Diagnosis
- History
- Distribution

Differential Diagnosis
- Mucosal melanotic macule
- Smoking-associated melanosis
- Superficial malignant melanoma

Treatment
- None

Prognosis
- Excellent
Smoker’s Melanosis

**Etiology**

- Melanin pigmentation of oral mucosa in heavy smokers
- May occur in up to 1 of 5 smokers, especially females taking birth control pills or hormone replacement
- Melanocytes stimulated by a component in tobacco smoke
Clinical Presentation

• Brownish discoloration of alveolar and attached labial gingiva, buccal mucosa
• Pigmentation is diffuse and uniformly distributed; symmetric gingival pigmentation occurs most often.
• Degree of pigmentation is positively influenced by female hormones (birth control pills, hormone replacement therapy).
Microscopic Findings

- Increased melanin in basal cell layer
- Increased melanin production by normal numbers of melanocytes
- Melanin incontinence
Diagnosis
• History of chronic, heavy smoking
• Biopsy
• Clinical appearance

Differential Diagnosis
• Physiologic pigmentation
• Addison’s disease
• Medication-related pigmentation (drug-induced pigmentation by chloroquine, clofazimine, mepacrine, chlorpromazine, quinidine, or zidovudine)
• Malignant melanoma
Treatment

• None
• Reversible, if smoking is discontinued

Prognosis

• Good, with smoking cessation
Peutz-Jeghers Syndrome

• Peutz-Jeghers syndrome is an autosomal-dominant trait that produces the general findings of skin and/or mucosal melanotic macules with intestinal polyposis.

• The polypoid lesions in this condition generally behave as benign lesions although patients with carcinoma arising from adenomatous polyps have been reported.

• Many of these polypoid lesions are thought to be of inflammatory or hamartomatous origin and are also occasionally associated with dermatologic or oral mucosal abnormalities.
Clinical Presentation

• In Peutz-Jeghers syndrome oral pigmentation is distinctive and is usually pathognomonic.
• Multiple focal melanotic brown macules are concentrated about the lips while the remaining facial skin is less strikingly involved.
• The macules appear as freckles or ephelides, usually measuring < 0.5 cm in diameter.
• Similar lesions may occur on the anterior tongue, buccal mucosa, and mucosal surface of the lips.
• Ephelides are also seen on the fingers and hands.
Peutz-Jeghers Syndrome

- Bluish black macules
- Skin pigment but not oral tends fade with age
- Intestinal polyp
Peutz-Jeghers syndroma – clinical findings
Intestinal findings
Diagnosis

- The number and locations of melanotic macules should be recorded and compared to the expected distribution.
- Upper and lower gastrointestinal dye radiologic series are required.
- Biopsy

Differential Diagnosis

- Addison disease
- Albright syndrome
- Hereditary neurofibromatosis
Treatment

• Because the malignant transformation incidence of adenomatous polyps is as high as 20% to 40%, flexible fiberoptic examinations and polyp biopsy also are valuable.

Prognosis

• Good, but intense long-term follow-up is required because of a malignancy rate that is higher than previously thought and possible gastrointestinal complications.
Amalgam tattoo

Intraoral brown and black conditions

Amalgam restoration

Amalgam retrograde filling
Local argyrosis
10 Habits That Are Really Bad For Your Teeth
http://www.portmanhealthcare.co.uk/10-habits-really-bad-teeth/

Chewing pencils
Intraoral brown and black lesions

Graphite Tattoo
ORAL TATTOO
Д.Е.Г.

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Intraoral brown and black conditions

Black Hairy Tongue
Varicoses

lingual varices
Vascular abnormalities

Vascular tumors
- Infantile hemangioma
- Congenital hemangioma
  - NICH
  - RICH

Vascular malformations
- Slow-flow
- Fast-flow
  - Arterial malformation (AM)
  - Arteriovenous fistula (AVF)
  - Arteriovenous malformation (AVM)

• Combined types
Hemangioma
Hemangioma
D.D with Hematoma!!!
D.D. By vitropresion
Miyazaki H. et al.  
Intralesional laser treatment of voluminous vascular lesions in the oral cavity  
Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics.  
2009, 107 (2):164 - 172
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Intralesional laser treatment of voluminous vascular lesions in the oral cavity  
Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics.  
2009, 107 (2):164 - 172
Наличие на системни изяви и симптоми!
Addison’s Disease

Pituitary Gland

Pituitary Gland

ACTH

Gluco-corticoid (Hydrocortisone)

Cause adrenal produce

Blood circulation

Into
Morbus Addisoni
What is this?
(erypition hematoma)
Post traumatic hyperpigmentation