Oral Premalignancy
**Premalignant lesion** is a morphologically altered tissue in which cancer is more likely to occur, than its apparently normal counterpart parts.

**Premalignant condition** is a generalized state or condition associated with significantly increased risk for cancer development.

Various oral mucosal lesions, particularly red lesions (erythroplakias) and some white lesions (leukoplakias), have a potential for malignant change.
## Risk factors for malignant change in white lesions

<table>
<thead>
<tr>
<th>History</th>
<th>Clinical aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betel quid usage</td>
<td>Advanced age</td>
</tr>
<tr>
<td>Tobacco smoking or snuff dipping&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Female gender&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>High alcohol intake</td>
<td>Areas of reddening in the lesion</td>
</tr>
<tr>
<td>Genetic disorders (see Ch. 17)</td>
<td>Areas of speckling in the lesion</td>
</tr>
<tr>
<td></td>
<td>Nodular areas or ulceration</td>
</tr>
<tr>
<td></td>
<td>High risk site:&lt;br&gt;posterolateral tongue&lt;br&gt;floor of mouth&lt;br&gt;retromolar region&lt;br&gt;anterior pillar of fauces</td>
</tr>
<tr>
<td></td>
<td>Large lesions</td>
</tr>
<tr>
<td></td>
<td>Lesions present for long periods</td>
</tr>
<tr>
<td></td>
<td>Enlargement or change in character of&lt;br&gt;pre-existing lesion</td>
</tr>
<tr>
<td>Special investigations</td>
<td>Degree of dysplasia on biopsy</td>
</tr>
</tbody>
</table>
Classification:

Premalignant lesions:

- Leukoplakia
- Erythroplakia
- Pipe smokers’ keratosis
- Snuff-dippers’ keratosis
- Carcinoma in situ
- Bowen disease
- Actinic keratosis

Contd....
Premalignant Conditions:
- Oral submucous fibrosis
- Tertiary syphilis
- Lichen planus
- Discoid lupus erythematosus
- Dyskeratosis congenita
- Sideropenic dysplasia
Lesions / Conditions with potential for malignant change

<table>
<thead>
<tr>
<th>Lesion/condition</th>
<th>Aetiology</th>
<th>Risk of malignant change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysplastic leukoplakia</td>
<td>Unknown</td>
<td>High, but can regress</td>
</tr>
<tr>
<td>Erythroplasia</td>
<td>Idiopathic/smoking</td>
<td>Very high</td>
</tr>
<tr>
<td>Speckled leukoplakia</td>
<td>Idiopathic/smoking</td>
<td>High</td>
</tr>
<tr>
<td>Tertiary syphilis</td>
<td>Treponema pallidum</td>
<td>Very high</td>
</tr>
<tr>
<td>Oral submucous fibrosis</td>
<td>‘Betel’ chewing</td>
<td>High</td>
</tr>
<tr>
<td>Dyskeratosis congenita</td>
<td>Genetic</td>
<td>High</td>
</tr>
<tr>
<td>Pipe smokers’ keratosis</td>
<td>Pipe smoking</td>
<td>Low and not in the keratotic area</td>
</tr>
<tr>
<td>Snuff-dippers’ keratosis</td>
<td>Smokeless tobacco</td>
<td>Low</td>
</tr>
<tr>
<td>Chronic candidosis</td>
<td>Candida albicans</td>
<td>Low</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>Idiopathic</td>
<td>Low</td>
</tr>
<tr>
<td>Discoid lupus erythematosus</td>
<td>Autoimmune</td>
<td>Unclear (mainly lip)</td>
</tr>
</tbody>
</table>

Risks of malignant change are difficult to determine accurately and vary with many factors discussed below. If more than 25% of lesions become malignant in 5 years this is considered an exceptionally high risk. Malignant change in 2–3% of lesions in 5 years is considered a relatively low risk. Note that the highest risk lesions are uncommon. Common lesions appear in between 1% and 5% of the population.
The best predictor of the potential for malignant transformation is the degree of dysplasia seen histologically. For this reason, and because a few lesions will already be malignant, biopsy of red and white patches is mandatory. The term dysplasia (literally, abnormal growth) is given to the cytological abnormalities seen in both malignant and premalignant cells. Premalignancy is distinguished from malignancy only by the latter’s invasiveness and release of metastases.
Epithelial dysplasia: histological features

• Drop-shaped rete ridges
• Nuclear hyperchromatism
• Nuclear pleomorphism
• Altered nuclear/cytoplasmic ratio
• Excess mitotic activity
• Loss of polarity of cells
• Deep cell keratinisation
• Disordered or loss of differentiation
• Loss of intercellular adherence
Mild dysplasia. In this lesion there is a thin layer of parakeratin and the structure, maturation and orderly differentiation of the epithelial cells is largely unaffected. However, there is a degree of irregularity of basal cells with variation in size and hyperchromatism.

Mild dysplasia. In this lesion there is prominent orthokeratosis and a keratohyaline layer immediately below it. Dysplasia is more prominent than in the previous figure, with enlarged hyperchromatic and bizarre cells in the basal and lower prickle cell layers.
Moderate dysplasia. The dermal papillae extend close to the surface and there are elongated rete processes, some of which are broader deeply. Enlarged and hyperchromatic cells are visible at this low power in rete processes and in most of the prickle cell layer.
Severe dysplasia. This rete process is composed almost entirely of cells with dark and irregularly shaped nuclei. Only the most superficial layers of cells show maturation to squamous cells and the orderly maturation and differentiation of epithelial cells has been lost.
Definition: A white hyperkeratotic, non-scrapable patch in the oral cavity which cannot be characterized as any other clinical entity and is always associated with tobacco intake. Definition does not carry any histological connotation with it.
Classification

Clinical
• Homogenous
  -Flat
  -Corrugated
  -Pumice like
  -Wrinkled
• Non Homogenous
  -Nodular / Speckled
  -Verrucous
  -Ulcerated
  -Erythroleukoplakia

According to extent
-Localized
-Diffuse

According to Banoczy
-Leukoplakia simplex
-Leukoplakia erosiva
-Leukoplakia verrucosa
Staging of Leukoplakia:

- **Size** - It is denoted by L
  - L1 — size < 2cm
  - L2 — size 2-4cm
  - L3 — size >4cm
  - Lx — size not specified

- **Clinical aspect** - Denoted by C
  - C1 — Homogenous
  - C2 — Non-homogenous
  - Cx — Not specified

- **Pathological aspect** - Denoted by P
  - P1 — No dysplasia
  - P2 — Mild dysplasia
  - P3 — Moderate dysplasia
  - P4 — Severe dysplasia
  - Px — Not specified
Etiopathogenesis

**LOCAL FACTORS**
- Tobacco
- Alcohol
- Chronic irritation
- Candidiasis
- Electromagnetic reaction or Galvanism

**REGIONAL AND SYSTEMIC FACTORS**
- Syphilis
- Vitamin deficiency
- Sideropenic anemia
- Nutritional deficiency
- Xerostomia
- Hormonal disorders
- Drugs
- Virus
- Actinic Radiation
Clinical features

- *Sex and distribution*
- *Common sites*
- *Appearance*
- *Surface*
- *Color*
- *Symptoms*
- *Sharp staging*
- *Ebbing tide type*
Homogeneous leukoplakia.
Sublingual Homogeneous leukoplakia
Sublingual Homogeneous Leukoplakia
Commissural Leukoplakia
Speckled leukoplakia.
Speckled leukoplakia
Nodular or speckled leukoplakia
Thick white plaque on the lateral border of tongue represents verrucous leukoplakia.
Erythroplakia.
Erythroplakia
Differential Diagnosis

- Lichen planus
- Chemical burns
- Syphilitic mucus patches
- White spongy nevus
- DLE
- Psoriasis
- Leukoedema
- Hairy leukoplakia
- Verruca vulgaris
- Verrucous carcinoma
- Electro galvanic lesion
- Chronic cheek biting
Management:

- Limitation of etiological factor
- Conservative treatment
  - Vitamin therapy (Vit.A 75000-3,00,000 IU)
  - Vit.A + Vit.E
  - 13-cis-retinoic acid
  - Antioxidant therapy
    - Lycopene 2-8mg/day for 2 months
    - Beta-carotene
    - Vit.A Palmitate
  - Vit.B complex
  - Antimycotic Tt. (Nystatin 5 lac IU bid +20% borax or 1% gentian violet)
  - Panthenol lingual tab
  - Estrogen
• **Surgical Management**
  - Conventional surgery
    - Excision
    - Mucosal flap
  - Cryosurgery
  - Fulguration (*electrosurgery or electrocautry*)
  - LASER
    - Biopsy
    - Laser peel
    - Ablation
    - Surface vaporization

• **Miscellaneous**
  - Radiation therapy
  - Topical chemotherapy (*Bleomycin, Azathiprine etc*)
LICHEN PLANUS

• Described in 1869 by Erasmus Wilson.

• Various mucosal surfaces involved.

• Common inflammatory disease of skin with characteristic violaceous, polygonal, pruritic papules.

• It also involves mucosa, nails & hair
Definition

Relatively common dermatological disorder occurring on skin and oral mucus membrane and refers to lace like pattern produced by symbolic algae and fungal colonies on the surface of rocks in nature (lichens).
Types:

- Reticular
- Papular
- Atrophic
- Erosive
- Bullous
- Annular
- Actinic
- Linear
- Hypertrophic
Etiology:

- Immunological
  - Cell mediated immune response
  - Autoimmunity
  - Immunodeficiency
- Genetic factors
- Infections
- Drugs and chemicals
- Psychogenic factor
- Habits
Clinical Features:

• **Age & Sex:** 35-55 Yrs ; F > M

• **Incidence & Prevalence:** 0.9 % - 1.2 %

• **Site:** Skin, oral & other mucus membranes. About 50% of skin cases have oral lesions, 25% only oral lesions

• **Oral and genital mucosal lesions:** ‘Vaginogingival syndrome’

• **Symptoms:** Intense pruritis (skin), Burning mouth

• **Signs:** Characteristic Six ‘P’; Planar, polygonal, purple, pruritic, papules & plaques.
Oral lichen planus

- Sites: Buccal mucosa (84%)
- Burning mouth
- Wickham’s striae
- Typical lacy, reticular patterns, rings over the buccal mucosa.
- Associated hyper melanosis
- Usually bilateral.
- Stress induced
Treatment:

• Medicinal therapy
  - Steroids
  - Antifungal agents
  - Vit.-A
  - Cyclosporine
  - Dapsone

• Surgical Therapy
• Psychotherapy
• PUVA Therapy
• Symptomatic treatment
Oral Submucous Fibrosis

- **Synonyms:** Asian sideropenic dysphagia, oral mucosal disease, oral fibrosis, OSMF, oral soft tissue disease.
Introduction

Diffuse firm whitish areas of submucosal scarring and fibrosis usually associated with frequent and prolonged contact with betel nut quids, tobacco, hot peppers and other synergistic events; lesions have a higher than normal risk of developing squamous cell carcinoma
## Geographic Distribution

<table>
<thead>
<tr>
<th>Primary locations</th>
<th>Other locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>China</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Thailand</td>
</tr>
<tr>
<td>Burma</td>
<td>Vietnam</td>
</tr>
</tbody>
</table>
Etiology - unknown?

Genetic
Infectious agents
Carcinogens

Nutritional factors
Immunologic factors
Autoimmune
Genetic

- Never identified but can’t be ruled out
- Chili consumption in Mexico & South America is higher yet OSF is not present
Infectious Agents

- Candida - only an association

- HSV1 - high titers have been found in OSF, isolation of virus specific proteins has been unsuccessful
Carcinogens

- Betel nut
  - Arecoline - stimulate fibroblast proliferation and collagen synthesis *in vitro*
  - Flavonoids & Tannins - Inhibit collagenase activity
Carcinogens_cont.

- Tobacco carcinogens
  - Polycyclic aromatic hydrocarbons
  - N-nitrosonornicotine
    Nicotine_Nitrosation occurs by salivary enzymes
Nutritional Factors

- Iron -
- Vitamin B12
- Folic acid
Immunologic factors

It has been shown that when immunosuppression has been present for significant periods of time, the likelihood of a malignant tumor appearing is enhanced, the same is true for patients with OSF.
Autoimmunity

- Originally termed "idiopathic scleroderma of the mouth"

- The well documented findings of clinical, immunologic, and histologic abnormalities in OSF and similar reports in other connective tissue disorders suggest a fundamental autoimmune basis for the disease
Clinical Presentation

Chief Complaints:
- Progressive stiffness of the cheeks, which inhibits the ability to open the mouth
- Burning sensation of the oral mucosa aggravated by spicy foods
Clinical Presentation

- complications
  - limitation of mouth opening
  - Protrusion of the tongue
  - difficulty in mastication, speech and swallowing
  - Loss of auditory acuity (eustachian tube stenosis)
  - Severe trismus (lock Jaw)
  - Malignancy transformation
Clinical Presentation

Appearance: blanching marble-like appearance, with vesicles, ulceration and petechiae occurring less common

Location: oral cavity and occasionally the pharynx
Symptoms of OSF

- Progressive inability to open the mouth (trismus) due to oral fibrosis and scarring
- Oral pain and burning sensation upon consumption of spicy foodstuffs

Other symptoms

- Change of gustatory sensation
- Hearing loss due to stenosis of the eustachian tubes
- Dryness of the mouth
- Nasal tonality to the voice
- Dysphagia to solids (if the esophagus is involved)
- Impaired mouth movements (eg, eating, whistling, blowing, sucking)
Staging of OSF

• **Stage 1**: Stomatitis includes erythematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentation, and mucosal petechia.

• **Stage 2**: Fibrosis occurs in ruptured vesicles and ulcers when they heal, which is the hallmark of this stage. Early lesions demonstrate blanching of the oral mucosa.

• **Stage 3**: Sequelae of OSF
  
  Speech and hearing deficits
  Leukoplakia
Initially- Chronic inflammatory cell infiltration of subepithelial connective tissues, containing a number of eosinophils which are seldom found in oral inflammation.
Pathology

- Advancing to-
- Fibroelastic transformation of the juxtaepithelial c.t. layer
- Atrophy or hyperplasia of the overlying epithelium
- Accumulation of hyalinized collagen beneath the basement membrane
- Progressive loss of vascularity and
Diffuse fibrosis and hyalinization of subepithelial stroma with few, small fibroblastic nuclei.
Malignancy Development

- 1986 Pindborg 7.6%
- Some studies show up to 30%
Differential Diagnosis

- An easy clinical diagnosis
- Oral manifestations of scleroderma - rare
- Anemic conditions - pale mucosa with pigmentation
- Leukoplakia - if blanching is well circumscribed
Lab Studies:

• No specific diagnostic tests are available for OSF. Some OSF studies report the following laboratory findings:
  • Decreased hemoglobin levels
  • Decreased iron levels
  • Decreased protein levels
  • Increased erythrocyte sedimentation rate (ESR)
  • Decreased vitamin B complex levels

Other Tests:

• Cytologic smears may be performed.
Treatment

• Medical Care
  – Steroids
  – Placental extracts
  – Hyaluronidase
  – IFN-\(\gamma\)
  – Antioxidants
Surgical Care:

• Simple excision of the fibrous bands

• Split-thickness skin grafting following bilateral temporalis myotomy or coronoidectomy

• Nasolabial flaps and lingual pedicle flaps
Patient Education

• Discontinue the habit

• Eliminate tobacco

• Avoid spicy foodstuffs

• Eat a complete and healthy diet

• Maintain proper oral hygiene

• Schedule regular oral examinations
Special Concerns

• An unhealing ulcer in the lesion
• Lesion undergoing red changes (erythroplakia)
• A burning sensation in the mouth
• An exophytic mass
• A lump in the neck
• Difficulty in chewing, swallowing, or speaking