Overview

- Squamous papilloma
- Smokeless tobacco keratosis
- Leukoplakia
- Squamous cell carcinoma
- Verrucous carcinoma

Squamous papilloma

- Benign proliferation of squamous cells
- Etiology: Presumably human papillomavirus (HPV)
  - HPV types 6 and 11 have been identified
- Gender: No gender predilection
- Age: Any age
- Site: Any oral site
  - Mostly tongue, lips, soft palate
- Clinical features:
  - White to pink
  - Soft, painless
  - Finger-like projections – “cauliflower-like”
Squamous papilloma

- **Differential diagnosis:**
  1) Verruca vulgaris (common wart)
     * At times, papillomas and warts can appear identical *
  2) Condyloma acuminatum
      - broader base
  3) Inflammatory papillary hyperplasia
      - under ill-fitting denture
  4) Verrucous carcinoma

Warts
- multiple

Condyloma acuminatum
- broad-based

Inflammatory papillary hyperplasia
- palate; more diffuse;
  under denture

Squamous papilloma

- **Histology:**
  - keratinized, stratified squamous epithelium
  - papillary configuration
  - fibrovascular connective tissue
  - variable inflammation

- **Treatment:** Conservative surgical excision

Smokeless tobacco keratosis

- **Etiology:**
  Habit of chewing or holding tobacco in oral cavity
  - allows absorption of nicotine and other carcinogens through oral mucosa

- **Age and gender:**
  Older and young males
  In some populations, females predominate
Smokeless tobacco keratosis

- **Clinical features:**
  - Thin, gray-white plaque
  - Velvety
  - Fissured, rippled
  - Older lesions: leathery or nodular
  - *Gingival recession; dental caries; staining*

Smokeless tobacco keratosis

- **Differential diagnosis:**
  1) Frictional hyperkeratosis
     - Cheek/lip biting
  2) Chemical injury / burn
  3) True leukoplakia
  4) Lichen planus
Smokeless tobacco keratosis

- **Histology**:
  - hyperkeratosis
  - parakeratin chevrons
  - thickened spinous layer (acanthosis)
  - amorphous material in connective tissue
  - (+) dysplasia, CIS, SCC

- **Treatment**:
  - Depends on histologic diagnosis
  - Risk of developing:
    1) **Squamous cell carcinoma**
       - risk 4x greater than non-smokeless tobacco users
       - if combined with betel quid, risk 10x greater
    2) **Verrucous carcinoma**
      - 98% of mild smokeless tobacco keratoses will resolve on cessation of habit *

Leukoplakia

- **Definition**:
  - "A white, plaque-like lesion which cannot be wiped off AND cannot be clinically diagnosed as any other disease entity"
  - **Clinical** term, not related to histopathology

- **Diagnosis of exclusion**
  - Must exclude clinically distinct entities
  1) Frictional (traumatic) keratosis
     - e.g. chronic cheek/lip biting
  2) Lichen planus
  3) Leukoedema
     - bilateral buccal mucosa; translucent
  4) Nicotine stomatitis
     - hard palate; mostly related to pipe smoking

- 5-25% of leukoplakias are diagnosed as **dysplasia** after microscopic examination
- 4% diagnosed as **squamous cell carcinoma (SCC)**

Therefore, true leukoplakias are considered to be **premalignant lesions**
Leukoplakia

• Proposed etiologies:
  1) Tobacco
     - large proportion of leukoplakias in smokers disappear after 1st year of smoking cessation
  2) Smokeless tobacco (tobacco pouch keratosis)
  3) Sanguinaria (sanguinaria-associated keratosis)
     - Viadent products
     - location: maxillary vestibule or alveolar mucosa
     - may not disappear after cessation of sanguinaria use

**Frictional keratosis – not true leukoplakias

Leukoplakia

• Gender: Male predilection
• Age: Older than 40 yo
• Site: Lip vermilion, bu mucosa, gingiva
  - Tongue, floor of mouth, lip vermilion - high risk areas for dysplasia
• Clinical features:
  - Gray to white plaques
  - Flat; slightly elevated; fissured
• Clinical variants:
  - Thin; thick; granular/modular; verrucous;
  - proliferative verrucous leukoplakia (PVL)
Leukoplakia

- **Differential diagnosis:**
  1) Frictional (traumatic) hyperkeratosis
  2) Linea alba
     - bilateral lines on buccal mucosa; level of occlusal plane
  3) Lichen planus
     - look for striations
  4) Chemical injuries
     - e.g. aspirin, hydrogen peroxide

Frictional Hyperkeratosis

Trauma
- from kissing!

Chemical injury
- aspirin burn
Leukoplakia

- **Histology:**
  - hyperkeratosis
  - acanthosis
  - + dysplasia; mild, moderate, severe
  - + carcinoma-in-situ (CIS)
  - + squamous cell carcinoma

- **Transformation to dysplasia rates:**
  - Thin leukoplakia – seldom (80% hyperkeratoses)
  - Thick leukoplakia – 1-7%
  - Granular leukoplakia – 4-15%

- **Transformation to SCC rates:**
  - Moderate dysplasia – 4-11%
  - Severe dysplasia – 20-35%
  - Usually 2-4 years after onset of leukoplakia
  - Risk increased if persistent lesion, female patient, nonsmoker, FOM or ventral tongue site

- **Treatment:**
  - Depends of histologic diagnosis
  1) If hyperkeratosis or mild dysplasia:
     - Clinical follow-up every 6 months
     - Complete removal (surgical, laser, etc)
  2) If moderate dysplasia or worse:
     - If high-risk area (floor of mouth, ventral or lateral tongue):
       - Complete removal (surgical, laser, etc)
     - Try to preserve specimen for histological exam

**Careful long-term follow-up**

Squamous cell carcinoma

- Malignant neoplasm of squamous cells
- **Incidence:**
  Oral cancer < 3% of all cancers in U.S.
  94% of oral cancers are SCC
  21,000 new cases diagnosed annually
- **Groups at risk:**
  Caucasian males, >65 yo; decreasing
  AA males, middle aged; increasing

- **Etiology:**
  **Multifactorial disease**
  Most preceded by leukoplakia or erythroplakia
  1. Tobacco smoking
  2. Smokeless (spit) tobacco
  3. Betel quid (paan)
  4. Alcohol
  5. Iron deficiency
  6. Immunosuppression
Squamous cell carcinoma

- pipe and cigar smoking, greater risk
- more cigarettes, greater risk
- reverse smoking, greater risk

• SCC that occurs in non-smokers
  - female
  - cancer of oral cavity (esp. tongue) vs. pharynx, larynx
  - young age

Squamous cell carcinoma

• Gender: M:F = 3:1
• Age: Older adults
• Site:
  - Intraoral – tongue; posterior lateral border, ventral
    - FOM > soft palate > gingiva > bu mucosa > la mucosa > hard palate
  * FOM SCC – high risk of second primary malignancy
  - Oropharyngeal – tonsil, posterior soft palate, base of tongue

Squamous cell carcinoma

• Site:
  - Lip vermillion
    - Risk factors – light-skinned
      - long-term exposure to sunlight
      - outdoor occupation
    - Site – lower lip

Squamous cell carcinoma

• Clinical features:
  May be painless
  Varied clinical appearance
  1. Growth pattern
     Exophytic, endophytic
  2. Surface characteristics
     Intact, ulcerated
     Granular, papillary
  3. Color
     White, red, mixed
Squamous cell carcinoma

• Radiographic features:
  May cause destruction of underlying bone
  Ill-defined radiolucency
  Can mimic periodontal disease

Squamous cell carcinoma

• Differential diagnosis:

Intraoral SCC
  1) Leukoplakia/erythroplakia
  2) Traumatic ulcer
  3) Ulcer of infectious origin (e.g. TB, syphilis, deep fungal)
  4) Other malignancies (e.g. primary, metastatic, lymphoma)
Squamous cell carcinoma

- **Histology:**
  - dysplastic epithelium
  - islands of invasive squamous cells

- **Grading:**
  1) Well-differentiated
  2) Moderately differentiated
  3) Poorly differentiated

**Treatment**
- Depends on clinical staging (size, nodal status, distant metastasis)
- Surgical resection + radiation therapy + chemotherapy + Neck dissection
- 5-year survival rates – 9-85%
- Risk for second primary
  - highest risk for smokers and drinkers
  - FOM location
  - usually within 3 years of initial malignancy

Verrucous carcinoma

- Malignant neoplasm of squamous cells
- Low-grade variant of SCC

- **Incidence:**
  1-10% of oral SCCs

- **Etiology / Risk factors:**
  Chewing tobacco use
  Snuff use
Verrucous carcinoma

- **Gender:** M>F
- **Age:** >55 yo
- **Site:** Mandibular vestibule, buccal mucosa, hard palate, gingiva
  - Site of tobacco placement
- **Clinical features:**
  - White, may be pink
  - Diffuse, painless
  - Thick mass with papillary projections

Verrucous carcinoma

- **Differential diagnosis:**
  1) Conventional squamous cell carcinoma
  2) Leukoplakia; proliferative verrucous leukoplakia (PVL)
  3) Traumatic lesion, factitial (self-induced) injury
  4) Smokeless tobacco keratosis
  5) Squamous papilloma, verruca vulgaris
Leukoplakia

**Frictional hyperkeratosis**
- tongue-biting

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**Verrucous carcinoma**

- **Histology:**
  - papillary surface
  - abundant keratin
  - wide, bulbous rete pegs
  - “pushing” invasion
  - little atypia
  * conventional SCC in 20% *

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**Verrucous carcinoma**

- **Treatment:**
  Surgical resection
  Radiation therapy less effective