NEOPLASMS OF THE SURFACE EPITHELIUM
(KERATINOCYTES)
Papillary Lesions
Keratinocyte Proliferations
Melanotic Lesions

Precancerous Lesions
Carcinomas
Melanomas
Normal Mucosa

Keratin layer
Spinous layer
Basal layer
Submucosal Connective Tissues
Epithelial Lesions

- Benign Surface Papillomas
- Premalignant Lesions
  - Oral
  - Skin
- Carcinoma
  - Squamous Cell, Verrucous
  - Basal Cell
- Benign Nevi
- Malignant Melanoma
Benign Oral Papillary and Verrucous Tumors

- Verruca vulgaris - HPV 2,4
- Squamous papilloma - HPV 6,11
  - solitary
- Condyloma acuminatum - HPV 6,11
  - Multiple
- Keratoacanthoma HPV ?
- Focal Epithelial Hyperplasia (Heck disease)
  - HPV 13,32
- Warty Dyskeratoma
Verruca vulgaris

- Clinical
- Histopath and DNA
Squamous Papilloma

- Clinical, Gross

- Histopathology
Condyloma Acuminatum

- Clinical
- Histopath & DNA
Condyloma
Focal Epithelial Hyperplasia
Heck Disease

- Predominantly a childhood HPV disease
- Multifocal papules and nodules, lips and buccal mucosa
- HPV 13, 32, viruses that only cause oral mucosal flat warts
- The phenotype may be seen in HIV infected patients
- Spontaneous regression occurs in 6-12 months without treatment
- Microscopic: Dome shaped exophytic proliferations of SSE, marked acanthosis, mitosoid (mitotic-like) bodies found in the mid-spinous layer
FEH in HIV+ Subjects
Keratoacanthoma

- A verrucous well circumscribed tumor of skin with self-limited growth
- Documented cases of spontaneous regression
- Microscopic: Abrupt cup-like borders, marked parakeratosis and acanthosis without cytologic atypia
- Treatment: simple excision
- Cases with atypia should be considered low grade squamous carcinomas
Keratoacanthoma
Verruciform Xanthoma

- A papillary lesions with keratosis
- Tends to occur on the gingiva and palate
- Benign lesion
- Equal sex distribution
- Microscopically: Hyperkeratosis, Papillary pattern, Xanthoma (foam cell histiocytes) within the submucosal papillae
Verruciform Xanthoma

Xanthoma cells
Warty Dyskeratoma

- An epithelial warty proliferation of skin or mucosa with distinct microscopic features
- A focal counterpart to Darier White disease (keratosis follicularis)
- Multiple, yet limited lesions are referred to as focal acantholytic dyskeratosis (Grover’s disease)
- Microscopic: Verrucous keratosis with villous rete pegs, acantholysis and dyskeratotic cells in spinous layer
Warty Dyskeratoma
Carcinogenesis – Oral Cancer

• Smoked Tobacco
• The Smokeless Tobacco Issue
• Alcohol
• Carcinogens
  – Polycyclic Hydrocarbons
  – Nitrosourias
• Human Papillomaviruses
Carcinogenesis

- **Oncogenes**
  - Growth Factors
  - Growth Factor Receptors
  - Internal Signaling Pathway Mediators

- **Tumor Suppressor Genes**
  - Apoptotic Pathway Mediators
  - Cell Cycle Regulatory proteins
Growth Factors → Growth Factor Receptor → Internal Signaling Pathways → Transcription Factors

ACTIVATION ONCOGENES

CELL CYCLE

TUMOR SUPPRESSOR GENES INHIBITION

p53
Rb
HPV and p53

• HPV 16
  – Present in some leukoplakias and SCCA
  – Present in >60% of tonsilar/tongue base SCCA

• P53
  – Mutated in >60% of oral SCCA
  – Inactivated/nonmutated in HPV associated SCCA
HPV

Early Late

E6

p53 degradation

p53

CELL CYCLE ACTIVATED

No Inhibition

p53 mutation
LEUKOPLAKIA

A Clinical Term
Variants of Leukoplakia

- Homogeneous
- Verrucous
- Speckled
Leukoplakia

- 20% precancerous change histologically
- Floor of the Mouth – 40% dysplastic
- 6% of all leukoplakias will progress to carcinoma within 5-7 years
Leukoplakia
Leukoplakia

White lesions that cannot be rubbed away
Leukoplakia
Leukoplakia - Snuff Keratosis
Toluidine Blue, detection of dysplasia

Application of dye

Acetic Acid

Dye retention
Tissue Sampling (BIOPSY)

Brush Biopsy

Punch Biopsy
Benign Keratosis

- hyperorthokeratosis
- hyperparakeratosis
- acanthosis
Histologic Spectrum of Leukoplakia

- Hyperorthokeratosis
- Hyperparakeratosis
- Acanthosis
Hyperkeratosis/Acanthosis
Grades of Epithelial Dysplasia
Histologic Spectrum of Leukoplakia

- Mild Dysplasia
- Moderate Dysplasia
- Severe Dysplasia
Histologic Spectrum of Leukoplakia

- Squamous Cell Carcinoma
Erythroplakia

- Velvety red patch of unknown etiology
- More rare than leukoplakia
- Soft Palate, Floor of Mouth, Lateral Tongue
- 90% chance for dysplasia
- Often mixed with leukoplakic areas
  - (Leukoerythroplakia)
  - (Speckled leukoplakia)
Erythroplakia
Erythroleukoplakia (Speckled)
Proliferative Verrucous Leukoplakia

- Predilection for elderly females
- Only 40% use tobacco
- Predilection for gingiva, mucobuccal fold
- Persistent and Diffuse
- High Recurrence
Proliferative Verrucous Leukoplakia
PVL
PVL - Histopathology

- Varies from verrucous hyperkeratosis to verrucous carcinoma, papillary squamous cancer and invasive carcinoma
Lichen Planus and Oral Cancer

- Oral LP occurs in .5% of the population

- PREVALENCE: 1-2% of patients with OLP develop oral cancer (1:100) over follow up periods of 5-10 years

- INDICIDENCE: Oral SCCA in US (35,000:298,000,000 or approximately 1.2/10,000 (.012%) Estimate over 10 year and 20 year follow up periods.

- ODDS RATIOS:*
  - 1 year Follow up 1.0%:0.012% > 83.3
  - 10 year Follow up 1.0%:0.12% > 8.3
  - 20 year Follow up 1.0%:0.23% > 4.3

*Oral Ca over 10 year period 350,000/298,000,000 (.12%)
*Oral CA over 20 year period 700,000/298,000,000 (.23%)
Squamous Cell Carcinoma

- Ulcerated, indurated, white/red, fixed tumefaction
- Anterior mouth: Well differentiated, good prognosis
- Posterior mouth: Less differentiated, poor prognosis
- Lateral tongue, floor of mouth are favored sites although SCCA can occur anywhere in the oral mucosa
- 70+% smoking and alcohol
- Tonsilar pillar, base of tongue: HPV 16
- Tumor suppressor gene mutations (p16, p53)
- Prognosis: no nodes>70% 5 year survival; + nodes> 35% 5 year survival
Squamous Cell Carcinoma
Squamous Cell Carcinoma
Papillary SCCA
Oral Squamous Cell Carcinoma
Cervical Node Metastasis
TNM classification for Head and Neck Cancer

- **T** = size of Primary Tumor
  - T0: no evidence of tumor
  - T1: carcinoma in situ
  - T2: 2 cm or less
  - T3: 2-4 cm
  - T4: invasion of adjacent tissues

- **N** = regional lymph node involvement
  - N0: no palpable nodes
  - N1: suspicious, palpable node ipsilateral
  - N2: suspicious, palpable node contralateral
  - N3: large fixed node

- **M** = distant metastasis
  - M0: no evidence of disease
  - M1: distant metastases present

Staging according to TNM classification:

- **Stage I**: T1NoMo
- **Stage II**: T2NoMo
- **Stage III**: T3NoMo, T1N1Mo, T2N1M0, T3N1Mo
- **Stage IV**: T1N2Mo, T1N3Mo, T2N2Mo, T2N3Mo, T3N2Mo, T3N3Mo, any case with M1
Keratoses of the Face & Lips

- Seborrheic Keratosis
- Actinic Keratosis
- Actinic Cheilitis
Skin Keratoses

- **Seborrheic Keratosis**
  - Elderly males, facial skin, brown oily
  - Not precancerous

- **Actinic Keratosis**
  - Elderly males, facial skin, red and scaley
  - Precancerous, squamous cell CA

- **Actinic Cheilitis**
  - Elderly males, lower lip, white lesion
  - Precancerous, squamous cell CA
Seborrheic Keratosis

- Clinical
- Histopathology
Actinic Cheilitis
Basal Cell Carcinoma

- Facial Skin
- Keratosis, Ulcer with rolled borders
- Elderly
- Actinic Radiation
- Nonmetastasizing
- Other adnexa (sebaceous, sweat, hair)
Basal Cell Carcinoma

- Cutaneous Ulcer
- Histopathology
Squamous Cell Carcinoma
Variants of SCCA

• Histologic Grade
  – Keratinizing
  – Nonkeratinizing

• Verrucous Carcinoma

• Spindle Cell Carcinoma
Clinical Features SCCA

- >50 years
- In nonsmokers - >50 years
- >80% smoke cigarettes
- Alcohol is a risk cofactor
- Lateral tongue, Floor of mouth
- Prognosis:
  - Anterior portion of mouth – better
  - Posterior portion of mouth - worse
Therapy for Oral Cancer

• Laser Ablation
• Surgical Excision
• Radiation Therapy
• Neck Node Management
  – Partial Lymph Node Dissection
  – Radical Lymph Node Dissection
  – Radiation to the Neck
MRI Imaging for Head and Neck Cancer
Histopathology SCCA

- Well differentiated
- Poorly differentiated
Verrucous Carcinoma

- Elderly
- White keratotic
- Cauliflower or “Verrucous”
- Noninvasive, pushing margins
- Parakeratin crypts
- Nonmetastasizing
Verrucous Carcinoma

- Clinical
- Histopathology
Benign Melanocytic Nevi

• Nevocellular
  – Junctional
  – Compound
  – Intradermal/Intramucosal
  – Specific Types (Ota, Ito)

• Blue Nevi
  – Common
  – Cellular
Cutaneous Nevi
ORAL NEVI

• All histologic types are seen
• Melanocytes are normally present in the basal layer
• Palate > Gingiva > Buccal Mucosa
• Malignant transformation is very rare
Oral Nevi
Nevi

- Junctional
- Intramucosal
Blue Nevus
MELANOTIC MACULE

• Oral Freckle or Ephelis
• Lips > Gingiva > Palate
• Basilar Melanosis
• Melanin Incontinence
• No Malignant Potential
Oral Melanotic Macule
"increased melanin synthesis"

Amalgam and Graphite Tattoos
"extrinsic pigments"
Melanotic Macule
Melanotic Macule

Basilar melanosis

S100 protein
Melanoacanthoma

• Most common among African descent individuals
• Focal pigmented macule or plaque
• Basilar melanocytic hyperplasia with dendritic cells in spinous layer
• Not premalignant
Melanoacanthoma
Malignant Melanoma

- Melanoma in situ
- Superficial Spreading
- Nodular
ORAL MUCOSAL MELANOMA

- Anterior Maxillary Gingiva > Palate
- More common in Japan
- Highly lethal, metastasize widely
- Not classifiable by Clark levels
Superficial Spreading Melanoma

- Clinical
- Histopathology
Nodular Melanoma

- Clinical
- Histopathology
Oral Melanoma

Superficial spreading
Oral Melanoma

Nodular
Cutaneous Melanoma
Clark Levels

Bresloev Scale is measured as depth of invasion in mm

Epithelium

I

II

III

IV

V

Papillary Dermis

Reticular Dermis

SubQ Fat

Thin Melanoma