

**Oral & Maxillofacial Pathology**  
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***Oral and Maxillofacial Pathology is the specialty of dentistry and pathology that deals with the nature, identification and management of diseases affecting the oral and maxillofacial regions.***

This complex region of the body is affected with local diseases of the oral soft tissues, tumors and developmental abnormalities of the jaws and teeth, as well as lesions of the mouth secondary to systemic disease. An attempt to concentrate on those disease processes that may be encountered frequently in clinical practice will be undertaken.

### **Odontogenic Cysts**

By definition an odontogenic cyst is a pathologic cavity in bone or soft tissue which is lined by epithelium of odontogenic origin and which usually contains fluid or semi-solid material.

#### **Dentigerous cyst**



The most common of the developmental cysts. Always associated with the crown of an unerupted tooth. Forms from accumulation of fluid between the forming crown and dental follicle containing reduced enamel epithelium. Can cause root resorption, tooth displacement and pain. The mandibular 3<sup>rd</sup> molars are the most commonly associated teeth followed by the maxillary canines. The histology is

that of an empty or clear fluid filled cyst which is lined by thin nonkeratinized epithelium. The lining may exhibit mucous prosoplasia or respiratory type cilia. While extremely rare, malignant transformation of the squamous epithelium has been documented. Also subsequent development of ameloblastoma and mucoepidermoid carcinoma from the cyst wall is reported.

#### **Odontogenic keratocyst (OKC)**



The most common multilocular radiolucency; lesions may displace teeth, cause root resorption, thin the bony cortex and on rare occasion perforate the cortical bone. Peak incidence is in the 2<sup>nd</sup> and 3<sup>rd</sup> decades with a slight male predilection. The mandible is affected twice as often as maxilla, with the angle and 3<sup>rd</sup> molar/ramus area being the most common sites. 25% of OKC will be multilocular, and approximately 40% will be

associated with an impacted tooth. Characteristic histology with the cyst lumen lined by a uniform, corrugated parakeratinized squamous epithelium roughly 6-10 cell thick. The basal cell layer exhibits palisaded, hyperchromatic nuclei. Keratinaceous debris often fills the cyst lumen. Daughter cysts may be present within the connective tissue wall and have been implicated as foretelling a greater risk for recurrence. Treatments range from enucleation with curettage to en bloc resection, with a recurrence rate of up to 40% with the more conservative modalities. OKC is a major component of the **Nevoid Basal Cell Carcinoma syndrome** and patients with multiple odontogenic keratocysts and/or young age at presentation must be evaluated for this condition.

### Odontogenic Tumors

All odontogenic tumors result from some manner of misdirected odontogenesis. Odontogenic tumors are much less common than odontogenic cysts and often demonstrate evidence of the inductive influence between odontogenic epithelium and the odontogenic ectomesenchyme as seen in normal odontogenesis. As a general rule, the less differentiated or primitive the odontogenic cell of origin, the more aggressive the resultant tumor behaves.

### Ameloblastoma



Represents the most common epithelial odontogenic tumor and the most clinically significant benign odontogenic neoplasm.

Arises from remnants of dental lamina. Most common during the third to fourth decade with no gender predilection. Some recent studies out of South Africa suggest a predilection for blacks. The mandible is site for 80% of lesions, with molar and ascending ramus the most common location. Ameloblastoma are

slow growing tumors, with unlimited growth potential, which can grossly expand the bony cortex. Tooth displacement, mobility and root resorption are commonly observed. Several histopathologic varieties exist including follicular (most common), plexiform, desmoplastic, acanthomatous, granular

cell, and basal cell patterns. The characteristic histologic features of ameloblastoma are: islands of neoplastic odontogenic epithelium encircled by basaloid cells with hyperchromatic and palisading nuclei; in addition the nuclei are polarized away from the basement membrane; and exhibit subnuclear vacuolization of the cytoplasm. However, the histologic pattern or subtype of the conventional ameloblastoma does not seem to affect treatment. Treatment is dependent on the size of the lesion, and ability of the patient to tolerate the procedure. In general, the more radical the surgery performed, the lower the recurrence rate. Recurrence rates with conservative curettage reach 90%. Radiation therapy has proven to be of little value except as palliative therapy and has led to adverse outcomes including osteoradionecrosis and malignant transformation of previously benign tumors. Life time follow-up is required, as tumor recurrence can occur up to 20 years later (average is 8 years).

### **Significant variants of ameloblastoma**

**Unicystic** variants of ameloblastoma generally occur in younger individuals (teens and young adults), present in a dentigerous cyst-like manner, and warrant conservative surgical therapy. Recurrence rate is in the 10-15% range.

**Ameloblastic carcinoma** occurs within the jaws, often after several unsuccessful attempts at resection of a benign ameloblastoma. The cells comprising the tumor islands show cytologic evidence of malignancy.

### **Calcifying epithelial odontogenic tumor (Pindborg tumor)**



First described by the late Dr. Jens Pindborg. It arises from the stratum intermedium of the enamel organ. Most lesions present in early adulthood (average age is 40). The mandibular premolar-molar region is most common location, with a very rare soft tissue-only variant reported. Radiographic presentation varies from a well-circumscribed unilocular radiolucency to a diffuse mixed density radiopacity with

calcifications. Lesions are often associated with an unerupted tooth. Histologically, the CEOT is characterized by sheets, nests and cords of squamous epithelium exhibiting pleomorphic, hyperchromatic nuclei with a granular eosinophilic cytoplasm, **often misdiagnosed as metastatic carcinoma**. Leisegang rings (concentric lamellar calcifications) and amyloid

can be identified within most tumors. Considered somewhat less aggressive than ameloblastoma, surgical excision or en bloc resection is usually curative, however a 15% recurrence rate is reported even following what was considered complete surgical removal by the surgeon.

## **Odontoma**



The odontoma is often divided into two distinct categories: complex or compound. The complex variety is composed of normally appearing enamel, dentin, and pulp which are distributed in an disorganized manner. It is frequently located between the roots of teeth in the posterior mandible.

The compound variant primarily presents in the anterior maxilla as multiple small "toothlets".

The odontoma is probably best classified as a hamartoma rather than a neoplasm. The average age of the patient at presentation is 15 years with a slight male predilection. Conservative curettage for either of the variants is the recommended treatment of choice.

## **Salivary Gland Pathology**

### **Salivary Gland System**

#### **Major**

3 large paired aggregations of exocrine glands

parotid  
submandibular (submaxillary)  
sublingual

#### **Minor**

small aggregates of glands scattered throughout the oral cavity

#### **Parotid Gland**

Develops from oral ectoderm, almost exclusively serous acini, weighs between 15-30 grams  
Superficial and deep lobes separated by the facial nerve  
Empties via Stensen's duct - 100% serous  
Contains lymphoid tissue (3-24 nodes), 90% of which located lateral to facial nerve  
Gland embraces internal jugular vein, external carotid artery, auriculotemporal branch of trigeminal nerve & **facial nerve**

### **Submandibular Gland** (submaxillary gland)

Develops from endoderm, 2nd largest weighing between 10-15 grams  
80% serous and 20% mucinous  
empties via Wharton's duct  
3-6 lymph nodes adjacent to gland  
Unlike the parotid, no major nerves course through the gland

### **Sublingual Gland**

Develops from endoderm, smallest of major glands weighing approximately 2 grams  
Mucus secreting cells predominate ~ 70%  
Empties via several ducts along sublingual fold  
    Bartholin's duct - largest - empties into submandibular duct at sublingual caruncle  
    Rivinus ducts - smaller ducts which open directly in oral cavity

### **Minor Glands**

Between 500 and 1,000 distinct glandular structures throughout oral cavity  
Location

buccal mucosa, lips, floor of mouth, hard and soft palates, tonsillar pillars, and tongue **Error! Bookmark not defined.**

Mostly unencapsulated and lie in close contact with surrounding structures (especially muscles of the tongue and lips)

Anterior hard palate and gingiva are devoid of salivary glands

Secretion is predominantly mucus

## **Clinical Features of Salivary Gland Tumors**

Asymptomatic swelling is most common presentation whether benign or malignant

    symptoms usually not impressive

    pain need not indicate malignancy

*paresthesia is a sign of malignancy*

        Facial nerve paralysis 12-14% parotid malignancies

        Suggests poor prognosis

        If paresthesia... think Adenoid Cystic Carcinoma

Tumor growth rate not necessarily a good indicator of benign or malignant  
Tumor fixation or ulceration is sign of possible malignancy  
Patients with history of prior irradiation are at increased risk for salivary gland tumors  
Patients with salivary gland malignancies have higher incidence of breast cancers

### **Surgical Treatment of Salivary Gland Tumors**

#### **PAROTID**

Partial parotidectomy with adequate margin of uninvolved gland is minimal therapy for benign or malignant parotid gland tumors  
Superficial lobectomy preferred for benign and low grade malignant tumors of superficial lobe  
Total parotidectomy for all primary high grade malignant tumors, primary benign tumors of deep lobe, recurrent benign or malignant parotid gland tumors

#### **SUBMANDIBULAR and SUBLINGUAL GLAND**

Total submandibular gland removal is recommended for all tumors located here  
Total sublingual gland removal indicated for any tumor in this location

#### **MINOR GLANDS**

Wide local excision for all benign and low grade malignancies in minor gland locations  
More radical excision for high grade minor gland tumors

### **Benign Salivary Gland Tumors**

#### **Mixed Tumor (Pleomorphic Adenoma)**

Most common salivary gland neoplasm  
Asymptomatic, slow growing, nodular swelling  
Average duration 6 years  
Slight female predilection  
Wide age range, peaks in 30-40 yr olds

#### **Histopathology**

Ductal, squamous, myxoid, chondroid, osseous and spindle cell features  
Two main cell types  
- Ductal epithelial cells and myoepithelial cells  
Primary tumor in major glands is usually a well- encapsulated single nodule but may be bosselated  
Minor gland primary may only be well circumscribed without capsule  
Recurrent tumors often multinodular, frequently myxoid and within fat or gland parenchyma

## **Papillary Cystadenoma Lymphomatosum (Warthin's Tumor)**

95% located in parotid gland

Predominately men over age 40

Average duration 3 years

Associated with smoking

Most likely of salivary gland tumors to be bilateral (10%) or associated with another tumor type

### **Histopathology**

papillary

cystic

lymphoid stroma

epithelial cells appear oncocytic with eosinophilic granular cytoplasm

If needle biopsy performed prior to excision, may exhibit squamous metaplasia

## **Malignant Salivary Gland Tumors**

### **Mucoepidermoid Carcinoma**

Most common salivary gland malignancy

Second most common salivary gland tumor

Low - intermediate - high grades

Represents:

20% of all minor gland tumors

10% of all parotid gland tumors

9% of all submandibular gland tumors

### **Histopathology**

mucus cells: + for mucicarmine, alcian blue, and PAS, diastase resistant

intermediate cells: small, basaloid or clear cell

epidermoid cells: squamous

other cell types seen: columnar cells

TALP (tumor associated lymphoid proliferation) confused with metastasis

### **Prognosis**

varies by grade, site and most important, stage

overall:

Low grade 5 year survival      85 - 100%

High grade 5 year survival      20 - 40%

### **Adenoid Cystic Carcinoma**

Incidence

10% minor gland tumors

12% submandibular gland tumors

2% parotid gland tumors

Pain and paresthesia in 25% - 33%

Typically most common in middle age years

## **Histopathology**

all types have small basophilic cells with hyperchromatic angular nuclei

neurotropism common

### **3 growth patterns:**

1. cribriform: Swiss cheese or telephone dial
2. tubular: single tubules may co-exist with cribriform
3. solid: nests and islands with minimal evidence of other patterns, demonstrates necrosis, pleomorphism and mitoses

## **Prognosis**

cribriform and tubular: slow relentless progression of tumor with 20% 20 year survival rate

recurrence generally indicates incurability

solid: most rapidly progress to death within 24 months having frequent recurrence and metastasis

## **Carcinoma-Ex-Mixed Tumor**

About 5% of all mixed tumors, 86% occur in the major glands

Rapid growth after long indolent course

Pain, paresthesia, fixation

Requires evidence of benign mixed tumor **and** features of malignancy

neural, glandular, lymphatic invasion, necrosis, pleomorphism, increased mitoses

## **Histopathology**

Only the epithelial component is malignant

Most common histologic pattern is that of poorly differentiated adenocarcinoma or squamous cell carcinoma

Occasionally mucoepidermoid carcinoma or adenoid cystic carcinoma features are seen

## **Obstructive Disorders**

### **Mucus Escape Reaction**

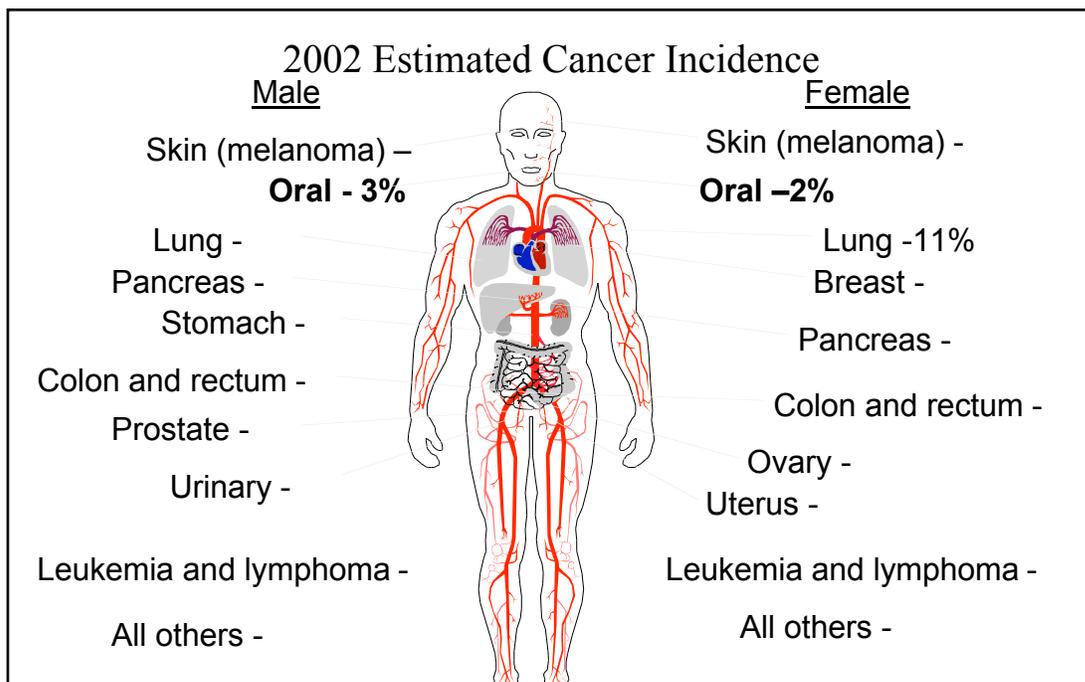
Mucocele - common lesion of the oral cavity - bluish dome shaped swelling

Results from traumatic rupture of a duct

Mucin spillage into surrounding tissue sets off granulation tissue response with neutrophils and foamy histiocytes  
 Chronic sialadenitis in adjacent salivary gland

## **ORAL CANCER Epidemiology**

1,284,900 new cancer cases in 2002 (637,500 male; 647,400 female)  
 29,900 new oral cancer cases in 2002 (2.3%)  
 Estimated cancer deaths in United States, 2002  
 555,500 deaths are expected (288,200 males, 267,300 females)  
 about 1,500 deaths each day  
 about 1 death each minute



## **ALCOHOL AND ORAL CANCER**

44% of patients with tongue cancer have hepatic cirrhosis

59% of patients with FOM cancer have hepatic cirrhosis

cirrhosis is found in 20-46% of patients with FOM cancer vs 9% of controls

## **TOBACCO - CIGARETTES**

Lethal packages exempt from federal laws that control hazardous substances

methyl isocyanate - poison

benzene - solvent

acetone - paint stripper

ammonia - clearing agent

arsenic - ant poison

cadmium - used in

rechargeable batteries

carbon monoxide - auto

exhaust

cyanide - rat poison

butane - lighter fluid

## **SMOKELESS TOBACCO**

- nitrosamines are very high, radioactive material may be present
- some reports of 50X increased risk for development of oral cancer but this topic is

controversial:

-> life expectancy of a 35-year-old smokeless tobacco user is 15 days less than non-user (smoker's is 7.8 years less)

-> Sweden has world's largest per capita ST consumer in 20th century yet their age-adjusted mortality rate from 1960-90 is low (2.3 to 3.6 per 100,000 person-years)

-> Swedish lung cancer mortality rates lowest in Europe over the past 40 years

## References:

Rodu B: An alternative approach to smoking control. Am J Med Sci 1994;308:32-34.

Rodu B, Cole P: Tobacco-related mortality. Nature 1994;370:184.

Vigneswaran N, Tilashalski K, Rodu B, Cole P: Tobacco use and

cancer. A reappraisal. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;80:178-182.

## **Clinical Appearance**

### **Leukoplakia**

*a white patch or plaque that cannot be characterized clinically or pathologically as any other disease*

- definition is based on exclusion of other lesions that may have similar clinical features. Concern is that some are premalignant or malignant lesions
- occurs in 50-70 year old age group
- high risk sites include floor of mouth, tongue, and lower lip
- microscopically
  - 80% benign
  - 12% mild to moderate dysplasia
  - 4% severe epithelial dysplasia
  - 3% squamous cell carcinoma
- 90% of those that show dysplasia or carcinoma occur on tongue, lip vermilion, and floor of mouth
- clinically may be opaque, translucent, fissured, wrinkled - terms applied have included *thin, homogeneous* or *thick, granular* or *nodular* and *verrucous*

### **Erythroplakia**

*defined as red patch that cannot be clinically or pathologically diagnosed as any other condition*

- much less common than leukoplakia but much more likely to be malignant or premalignant
- usually asymptomatic, well-demarcated erythematous macule or plaque (often associated with white element)
- histo: about 90% are dysplastic or carcinoma; atrophic epithelium with little keratin
- tx: if there is no obvious cause of irritation that might explain red lesion, must be biopsied

### **Epithelial Dysplasia**

#### **Histologic features:**

enlarged nuclei and cells with pleomorphism  
large and prominent nucleoli  
increased nuclear/cytoplasmic ratio  
hyperchromatic nuclei  
dyskeratosis  
increased mitotic activity and/or abnormal mitotic figures

if changes involve entire thickness of epithelium, diagnosis is carcinoma *in situ*  
invasive carcinoma reveals islands infiltrating lamina propria

### **Actinic Keratosis & Actinic Cheilosis**

pre-malignant skin or lip lesions caused by ultraviolet light, especially in fair-skinned people

face and neck, dorsum of hands, scalp, and lower lip are common sites

lesions are scaly, white, gray or brown plaques; male predilection; develop slowly

early changes in the lip include blotchy area and blurring of zone between vermilion and skin of lip

histo: atrophic epithelium, hyperkeratosis, solar elastosis, and dysplastic or carcinomatous epithelium

excision; for lip, vermillionectomy is often performed

lesion is preventable with adequate sun protection

### **Squamous Cell Carcinoma**

#### **Histologic Variants**

Verrucous carcinoma / proliferative verrucous leukoplakia

Spindle cell carcinoma

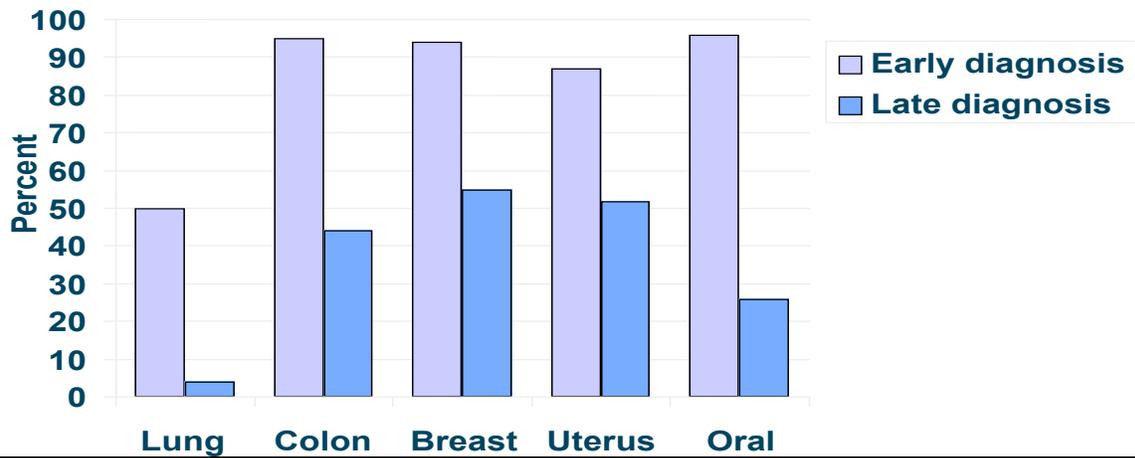
Basaloid squamous cell carcinoma

### **SPREAD OF DISEASE**

- usually NOT early with oral sites but oropharyngeal sites are prone to early mets
- mostly through lymphatics to ipsilateral cervical lymph nodes; contralateral nodes affected in some patients
- distant metastases most common to lungs, liver, bones
- carcinoma of lower lip & oral FOM to submental nodes whereas posterior oral carcinoma to superior jugular and digastric nodes

### **Influence of Early Detection on Five-year Survival**

## FIVE-YEAR SURVIVAL RATES BY SITE



### Oral Five-year Survival Rates

## Major sites: 5-year survival

