Oral cavity and salivary glands

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Acknowledgement and Disclosure Statements

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Overview

• Oral cavity
  • Diseases of the teeth and supporting structures
  • Inflammatory /reactive lesions
  • Infections
  • Oral manifestations of systemic disease
  • Precancerous and cancerous lesions
  • Odontogenic cysts and tumors

• Salivary glands
  • Xerostomia and Sialadenitis
  • Neoplasms of salivary glands
Oral Cavity– Diseases of Teeth and Supporting Structures

• Caries (tooth decay)
• Gingivitis
• Periodontitis
Caries (tooth decay)

• Dental caries is caused by focal demineralization of tooth structure (enamel and dentin) by acidic metabolites of fermenting sugars that are produced by bacteria.

• Represents primary cause tooth loss in persons younger than 35 years old.

• Prevention is achieved by improved oral hygiene and fluoridation of drinking water.
Gingivitis

- **Gingivitis** is the inflammation of the oral mucosa surrounding teeth; it is reversible.
- It is the result of poor oral hygiene and leads to accumulation of dental plaque and calculus.
- **Dental plaque** is a sticky, colorless biofilm that collects between the surface of the teeth; it contains bacteria, salivary proteins and desquamated epithelial cells.
- With time, plaque may become mineralized to form calculus (**tartar**).
Periodontitis

- **Periodontitis** is an inflammatory process that affects the supporting structures of the teeth (periodontal ligaments) alveolar bone and cementum, and may lead to loss of teeth.
- Poor oral hygiene with a shift in bacterial flora are important in the pathogenesis.
- May be associated with systemic disease (e.g. AIDS, leukemia, Crohn disease)
- May be the source of important systemic diseases (infective endocarditis, and pulmonary and brain abscesses).
Oral Cavity: Inflammatory/Reactive Lesions

- Apthous ulcers (canker sores)
- Fibrous proliferative lesions
Aphthous ulcers (canker sores)

- **Aphthous ulcers** are common, often recurrent, exceedingly **painful**, superficial oral mucosal ulcerations of **unknown etiology**.
- Affect up to 40% of the population and are common in the first 2 decades of life.
- May be associated with immunological disorders (e.g. celiac disease, IBD, Behcet dz).
- Lesions resolve spontaneously in 7 to 10 days.
Fibrous proliferative lesions

- Traumatic fibroma
- Pyogenic granuloma
- Peripheral ossifying fibroma
- Peripheral giant cell granuloma
Traumatic fibroma

• Submucosal nodular mass of fibrous connective tissue stroma that occurs on the buccal mucosa along the bite line, secondary to repetitive trauma.
Pyogenic granuloma

- Inflammatory lesion commonly found on the gingiva of children, young adults and pregnant women, characterized by an ulcerated and exophytic vascular proliferation, best treated by surgery.
Peripheral ossifying fibroma

- Common gingival growth
- Peak incidence in young and teenage females
- Likely reactive and not neoplastic
- Recurrence rate of 15-20%
- Treatment: Surgical removal
Peripheral giant cell granuloma

• Uncommon gingival growth
• Reactive and not neoplastic
• More common in adult females
• Treatment: Surgical removal
• Proliferation of multinucleated giant cells
Oral Cavity: Infections

• Herpes simplex virus infections
• Oral candidiasis (thrush)
• Deep fungal infections
Herpes simplex virus infections

• Oral herpes: **HSV-1 > HSV-2**
• Genital herpes: HSV-2 > HSV-1
• Primary oral HSV-1 infections typically occur in 2-4 y/o children, and are mostly asymptomatic.
• Most adults harbor latent HSV-1; reactivation (recurrent herpetic stomatitis) occurs in some.
• Clinically, lesions appear as groups of small vesicles on the lips.
Herpes simplex infection
Herpes simplex virus infections

- Histology of HSV infection:
  - Infected epithelial cells show intranuclear inclusions (three Ms).
  - Multinucleation
  - Nuclear Molding
  - Margination of chromatin
Oral candidiasis (thrush)

• *Candida albicans* is a normal component of the oral flora in 50% of the population.
• Most common fungal infection in the oral cavity.
• Three clinical types of oral candidiasis:
  – Pseudomembranous (aka thrush) most common
  – Erythematous
  – Hyperplastic
• Immune status has influence on likelihood of infection.
Candidiasis
Deep fungal infections

- Certain fungal infections show a predilection for the oral cavity and head and neck region.
- e.g. histoplasmosis, blastomycosis, coccidioidomycosis, cryptococcosis, zygomycosis and aspergillosis.
- With more immunocompromised patients, revalence of fungal infections of the oral cavity has increased in recent years.
Oral Cavity: Manifestations of Systemic Diseases

• Hairy Leukoplakia
• Infectious diseases
  – e.g. scarlet fever, measles, mononucleosis, HIV
• Dermatologic conditions
  – e.g. lichen planus, pemphigus, pemphigoid, SJS
• Hematologic disorders
  – Pancytopenia, leukemia, monocytic leukemia
Hairy Leukoplakia

- Distinctive oral lesion on the lateral border of the tongue seen, in the immunocompromised and caused by Epstein-Barr virus.

- Characterized by white, confluent patches of fluffy ("hairy") hyperkeratotic thickening.
Oral Cavity: Precancerous and Cancerous Lesions

- Leukoplakia and erythroplakia
- Squamous cell carcinoma
Leukoplakia and erythroplakia

Oral mucosal lesions that may undergo malignant transformation.
Leukoplakia and erythroplakia

- **Leukoplakia** is a white patch or plaque that cannot be scraped-off and cannot be characterized clinically or pathologically as any other disease.
- White plaques caused by irritation, lichen planus or candidiasis are not leukoplakia.
- All leukoplakias are considered precancerous until proven otherwise by histopathology.
Leukoplakia
Leukoplakia and erythroplakia

- **Erythroplakia** is much less common; it is a red, velvety, sometimes eroded area within the oral cavity.
- Risk of malignant transformation is higher.
Squamous cell carcinoma

95% of cancers of the head and neck are squamous cell carcinomas (SCC); most of the remainder are adenocarcinomas of the salivary glands.
Squamous cell carcinoma

• Pathogenesis of SCC
  – North America and Europe: middle aged individuals who smoke tobacco and abuse alcohol
  – Actinic radiation and smoking pipe are predisposing factors in SCC of the lower lip
  – India and Asia: Associated with chewing betel quid and paan.

  Areca nut
  Lime
  Tobacco
  Wrapped in betel leaf
Squamous cell carcinoma

• In the oropharynx as many as 70% of SCCs, particularly those involving the tonsils, the base of the tongue, and the pharynx, harbor oncogenic variants of HPV, particularly HPV-16.

• By 2020 the incidence of oropharyngeal SCC will surpass that of cancer of the uterine cervix.

• Patients with HPV-positive SCC of the oropharynx have a greater long term survival than those with HPV-negative tumors.
Squamous cell carcinoma

Development of SCC is driven by the accumulation of mutations and epigenetic changes that alter the expression and function of oncogenes and tumor suppressor genes, leading to acquisition of cancer hallmarks, such as resistance to cell death, increased proliferation, induction of angiogenesis and ability to invade and metastasize.
Squamous cell carcinoma
Oral Cavity: Odontogenic cysts and tumors

• **Odontogenic cysts** (derived from remnants of odontogenic epithelium within the jaws).
  – Dentigerous cyst
  – Odontogenic keratocyst
  – Periapical cyst

• **Odontogenic tumors**
  – Ameloblastoma
  – Odontoma
Odontogenic cysts

• **Dentigerous cyst**
  
  – Unilocular cyst
  – Originates around the crown of an unerupted tooth.
  – Often involving impacted third molar (wisdom) teeth.
  – Lined by a thin layer of stratified squamous epithelium.
  – Complete removal is curative
Odontogenic cysts

• **Odontogenic keratocyst (OKC)**
  
  – More common in the posterior mandible of male patients between 10 and 40 years old.
  
  – Unilocular or multilocular radiolucencies.
  
  – Lined by a thin layer of keratinized stratified squamous epithelium.
  
  – Multiple OKCs can occur nevoid basal cell carcinoma syndrome (Gorlin’s syndrome), associated with mutations in PTCH gene.
  
  – Treatment requires excision as OKCs are locally aggressive and may recur if not completely removed.
Odontogenic cysts

• Periapical cyst
  – Develops as a result of longstanding inflammation of the tooth (pulpitis), secondary to caries or trauma.
  – Inflammation leads to necrosis of pulp; may track down root and exit into surrounding alveolar bone.
  – Epithelialization of the cavity results in formation of periapical cyst.
Odontogenic tumors

• Diverse group of lesions; Some are hamartomas, others are true neoplasms (benign or malignant).
• Derived from odontogenic epithelium, ectomesenchyme, or both.
• **Ameloblastoma**: arises from odontogenic epithelium; has no ectomesenchymal differentiation.
  – Indolent but locally invasive; requires wide surgical excision.
• **Odontoma**: most common type of odontogenic tumor.
  – Arises from epithelium, but shows extensive deposition of enamel and dentin.
  – Probably represent hamartoma and not true neoplasm.
Odontogenic tumors

Ameloblastoma

Odontoma
Salivary glands

• There are three major salivary glands:
  - Parotid
  - Submandibular
  - Sublingual

• There are innumerable minor salivary glands throughout the mucosa of the oral cavity.
• Inflammatory and neoplastic diseases may develop within any of them.
Salivary Glands: Xerostomia

• **Xerostomia** is defined as dry mouth resulting from a decrease in the production of saliva.
• It is a major feature of **Sjogren syndrome**.
• Most frequently encountered as a **side effect** of many commonly prescribed medications.
• Complications include increased rate of dental caries, candidiasis and difficulty swallowing and speaking.
Salivary Glands: Inflammation (Sialadenitis)

• Sialadenitis may be caused by
  – **Trauma** (e.g. Mucocele)
  – **Viral or bacterial infections** (e.g. Mumps)
  – **Autoimmune disease** (e.g. Sjogren syndrome)
Sialadenitis secondary to Trauma

- **Mucocele** is the most common type of inflammatory salivary gland lesion; results from blockage or rupture of a salivary gland duct with leakage of saliva into connective tissue.
Sialadenitis secondary to infection

• **Mumps** is the most common form of viral sialadenitis; affects predominantly the parotid gland.
Salivary Glands: Neoplasms

• Salivary glands give rise to no fewer than 30 histologically distinct tumors.

• A small number of neoplasms make up more than 90% of salivary gland tumors.

• Parotid gland is most commonly involved (65-85% of cases)
# Salivary Gland Neoplasms

## Benign
- **Pleomorphic adenoma** (aka mixed tumor) (50%)
- **Warthin Tumor** (5-10%)
- Oncocytoma (1%)
- Other adenomas (5-10%)
  - Basal cell adenoma
  - Canalicular adenoma
- Ductal papillomas

## Malignant
- **Mucoepidermoid carcinoma** (15%)
- Adenocarcinoma (NOS) (10%)
- **Acinic cell carcinoma** (5%)
- **Adenoid cystic carcinoma** (5%)
- Malignant mixed tumor (3-5%)
- Squamous cell carcinoma (1%)
- Other carcinomas (2%)
# Salivary Gland Neoplasms

<table>
<thead>
<tr>
<th>Salivary Gland</th>
<th>Malignancy Rate</th>
<th>Incidence of Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>Submandibular</td>
<td>50%</td>
<td>15%</td>
</tr>
<tr>
<td>Sublingual &amp; Minor</td>
<td>70%</td>
<td>5%</td>
</tr>
</tbody>
</table>
Pleomorphic adenoma

- **Pleomorphic adenomas** are benign tumors that consist of a mixture of *ductal* (epithelial) and *myoepithelial cells*, and show both *epithelial* and *mesenchymal* differentiation.
- Most common salivary gland tumor; develop most often in the parotid.
- Recurrence: 4% after parotidectomy; 25% after simple enucleation.
- **Pleomorphic adenomas may undergo malignant transformation (carcinoma ex pleomorphic adenoma).**
Warthin tumor (papillary cystadenoma lymphomatosum)

- 2\textsuperscript{nd} most common salivary gland tumor; M > F 5\textsuperscript{th}-7\textsuperscript{th} decade.
- Almost exclusive to the parotid gland; may be bilateral.
- Smoking increases risk 8X

- Epithelial component is neoplastic
- Lymphoid component is reactive
- Benign tumor with a recurrence rate of 2%
Mucoepidermoid carcinoma

• Most common form of primary malignant salivary gland tumor.
• Represent about 15% of all salivary gland tumors, and occur mainly in the parotid (60-70%), but account for large fraction of minor salivary gland tumors.

• They are composed of squamous cells, mucous secreting cells and intermediate cells.
• May be sub-classified into low, intermediate or high-grade types; prognosis depends on its grade.
Adenoid cystic carcinoma

- Relatively uncommon, but distinctive carcinoma of the salivary glands.
- Involves minor salivary glands in 50% of cases.
- Are slow growing, unpredictable and stubbornly recurrent.
- Eventually 50% or more disseminate widely to distant sites.
- Five year survival is 60-70%
- Ten year survival is 30%; Fifteen year survival is 15%
Acinic cell carcinoma

• Composed of cells resembling normal *serous* acinar cells of salivary glands.
• Arise more commonly in the parotid glands; may be bilateral.
• Recurrence is uncommon;
• 10%-15% metastasize to lymph nodes.
• Five year survival rate is at 90%
• Twenty year survival rate is at 60%