Diseases of oral cavity
• Diseases of Teeth and Supporting Structures
• Inflammatory/Reactive Lesions
• Infections
• Oral Manifestations of Systemic Disease
• Precancerous and Cancerous Lesions
• Odontogenic Cysts and Tumors
• salivary glands disease
Inflammatory/Reactive Lesions

- **Aphthous Ulcers** (Canker Sores):
  - common, often recurrent, painful, superficial oral mucosal ulcerations
  - unknown etiology
  - most common in the first 2 decades of life.
  - tend to be prevalent within certain families
  - may also be associated with immunologic disorders including celiac disease, inflammatory bowel disease, and Behçet disease.
  - The lesions appear as single or multiple
  - The lesions typically resolve spontaneously in 7 to 10 days, but may sometimes persist for weeks, particularly in immunocompromised patients.
Figure 16-1 Aphthous ulcer. Single ulceration with an erythematous halo surrounding a yellowish fibrinopurulent membrane.
• irritation fibroma:
  - also called traumatic fibroma
  - occurs primarily on the buccal mucosa along the bite line or the gingiva
  - It is believed to be a reactive proliferation caused by repetitive trauma.
  - Treatment is complete surgical excision.
Figure 16-2 Fibroma. Smooth pink exophytic nodule on the buccal mucosa.
Figure 16-3 Pyogenic granuloma. Erythematous, hemorrhagic, and exophytic mass arising from the gingival mucosa.
Oral Manifestations of Systemic Disease

- **Hairy Leukoplakia:**
  - is a distinctive oral lesion on the lateral border of the tongue that is usually seen in immunocompromised patients (cancer therapy, transplant associated immunosuppression, advancing age, HIV)
  - is caused by Epstein-Barr virus (EBV).
  - It can be observed in patients infected with the human immunodeficiency virus (HIV) and may portend the development of AIDS.
  - takes the form of white, confluent patches of fluffy (“hairy”), hyperkeratotic thickenings, almost always situated on the lateral border of the tongue. Unlike thrush, the lesion cannot be scraped off.
Precancerous and Cancerous Lesions

• Leukoplakia:
  - defined by the WHO as “a white patch or plaque that cannot be scraped off and cannot be characterized clinically or pathologically as any other disease.”
  - This clinical term is reserved for lesions that are present in the oral cavity for no apparent reason.
  - 5% to 25% of these lesions are premalignant. Thus, until proven otherwise by means of histologic evaluation, all leukoplakias must be considered precancerous.
  - On histologic examination they present a spectrum of epithelial changes ranging from hyperkeratosis overlying a thickened, acanthotic but orderly mucosal epithelium to lesions with markedly dysplastic changes sometimes merging into carcinoma in situ.
Figure 16-5 Leukoplakia. A, Clinical appearance of leukoplakias is highly variable. In this example, the lesion is relatively smooth and thin with well-demarcated borders. B, The histologic appearance of a leukoplakia showing severe dysplasia that is characterized by nuclear and cellular pleomorphism, numerous mitotic figures, and a loss of normal maturation.
• **Erythroplakia:**
  - less common
  - The risk of malignant transformation is much higher than in leukoplakia.
  - The histologic changes in erythroplakia only rarely demonstrate orderly epidermal maturation; virtually all (approximately 90%) disclose severe dysplasia, carcinoma in situ, or minimally invasive carcinoma.
  - Often, an intense subepithelial inflammatory reaction with vascular dilation is seen that likely contributes to the reddish clinical appearance.

**Speckled leukoerythroplakia:**
Intermediate forms that have the characteristics of both leukoplakia and erythroplakia.
Figure 16-4 Erythroplakia. A, Lesion of the maxillary gingiva. B, Red lesion of the mandibular alveolar ridge. Biopsy of both lesions revealed carcinoma in situ.
Erythroplakia/Leukoplakia

- they are usually found in persons aged 40 to 70
- 2:1 male preponderance.
- Although these lesions have multifactorial origins, the use of tobacco (cigarettes, pipes, cigars, and certain forms of smokeless tobacco) is a common antecedent.
Squamous Cell Carcinoma

- Approximately 95% of cancers of the head and neck are squamous cell carcinomas (SCCs), with the remainder largely consisting of adenocarcinomas of salivary gland origin.
- Head and neck squamous cell carcinoma is the sixth most common neoplasm in the world
The pathogenesis of squamous cell carcinoma is multifactorial:

- Within North America and Europe:
a disease of middle-aged individuals
chronic abusers of smoked tobacco and alcohol.

- In India and Asia:
the chewing of betel quid and paan (areca nut, slaked lime, and tobacco, wrapped in a betel leaf) is a major regional predisposing influence.

- Actinic radiation (sunlight) and, particularly, pipe smoking are known predisposing influences for cancer of the lower lip.

- 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. Unlike the oropharynx, HPV-associated SCC of the oral cavity is relatively uncommon.
• The incidence of oral cavity SCC in individuals younger than age 40, who have no known risk factors (nonsmokers and not infected with (HPV)), has been on the rise. The pathogenesis in this group is unknown.
• Survival is dependent on a number of factors including the specific etiology of SCC.
• The 5-year survival rate of “classic” (smoking and alcohol related) early-stage SCC is approximately 80%, while survival drops to 20% for late-stage disease.
• Patients with HPV-positive SCC have greater long-term survival than those with HPV-negative tumors.
• The frequent development of multiple primary tumors markedly decreases survival.
• “field cancerization,” which postulates that multiple individual primary tumors develop independently in the upper aerodigestive tract as a result of years of chronic exposure of the mucosa to carcinogens.

• An alternative hypotheses to explain multiple “primary” tumors is that they are actually intraepithelial metastases.
Molecular Biology of Squamous Cell Carcinoma:
As with other cancers, the 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 the ability to invade and metastasize.

Tobacco carcinogen induced cancers:
mutations frequently involve the p53 pathway as well as proteins responsible for the regulation of squamous differentiation, such as p63 and NOTCH 1.

HPV-associated SCCs:
contain far fewer and different genetic alterations and typically overexpress p16, a cyclindependent kinase inhibitor. expression of the HPV oncoproteins E6 and E7, there is inactivation of the p53 and RB pathways
Figure 16-6 Clinical, histologic, and molecular progression of oral cancer. A, An idealized representation of the clinical progression of oral cancer. B, The histologic progression of squamous epithelium from normal, to hyperkeratosis, to mild/moderate dysplasia, to severe dysplasia, to cancer. C, The sites of the most common genetic alterations identified as important for cancer development. CIS, Carcinoma in situ; SCC, squamous cell carcinoma. (Clinical photographs courtesy of Sol Silverman, MD, from Silverman S: Oral Cancer. Hamilton, Ontario, Canada, BD Dekker, 2003.)
• MORPHOLOGY:
For the “classic” oral cavity SCC, the favored locations are the:
ventral surface of the tongue
floor of the mouth
lower lip
Soft palate
Gingiva
typically preceded by the presence of premalignant lesions
Figure 16-7 Squamous cell carcinoma. A, Clinical appearance demonstrating ulceration and induration of the oral mucosa. B, Histologic appearance demonstrating numerous nests and islands of malignant keratinocytes invading the underlying connective tissue stroma and skeletal muscle.
• the degree of histologic differentiation, as determined by the relative degree of keratinization, is not correlated with behavior.

• these tumors tend to infiltrate locally before they metastasize to other sites.

• The favored sites of local metastasis are the cervical lymph nodes, while the most common sites of distant metastasis are mediastinal lymph nodes, lungs, liver, and bones.

• Unfortunately, such distant metastases are often already present at the time of discovery of the primary lesion.
SALIVARY GLANDS

• Xerostomia:
  - dry mouth
  - resulting from a decrease in the production of saliva.
  - It is a major feature of the autoimmune disorder
    **Sjögren syndrome**, in which it is usually accompanied by dry eyes (keratoconjunctivitis sicca).
  - Other causes: radiation therapy, medications
  - Complications: dental caries, candidiasis, difficulty in swallowing and speaking.
• Inflammation (Sialadenitis):
Causes: - trauma
    - viral infection (Mumps---parotids)
    - bacterial infection
    - autoimmune disease
- **Mucocele:**  
  - The most common type of inflammatory salivary gland lesion.  
  - It results from either blockage or rupture of a salivary gland duct, with consequent leakage of saliva into the surrounding connective tissue stroma.  
  - Most often found on the lower lip and are the result of trauma.  
  - Patients may report a history of changes in the size of the lesion, particularly in association with meals.  
  - Complete excision of the cyst and its accompanying minor salivary gland lobule is required, as incomplete excision may lead to recurrence.  
  - **Ranula** is a term reserved for epithelial-lined cysts that arise when the duct of the sublingual gland has been damaged.
Figure 16-14 Mucocele. **A**, Fluctuant fluid-filled lesion on the lower lip subsequent to trauma. **B**, Cystlike cavity filled with mucinous material and lined by organizing granulation tissue.
• **Nonspecific Sialadenitis:**
  - Most often involving the major salivary glands, particularly the *submandibular glands*.
  - Usually secondary to ductal obstruction produced by stones (*sialolithiasis*)---- The stone formation is sometimes related to obstruction of the orifices of the salivary glands by impacted food debris or by edema about the orifice after some injury.
  - The common offenders are **S. aureus** and **Streptococcus viridans**.
  - Unilateral involvement of a single gland is the rule.
  - Other causes: Decreased secretory function (phenothiazines, dehydration--- elderly/major surgery)
Neoplasms

• these neoplasms are relatively uncommon and represent less than 2% of all tumors in humans.
• 65% to 80% arise within the parotid, 10% in the submandibular gland, and the remainder in the minor salivary glands.
• 15% to 30% of tumors in the parotid glands are malignant. In contrast, approximately 40% of submandibular, 50% of minor salivary gland, and 70% to 90% of sublingual tumors are cancerous. Thus, the likelihood of a salivary gland tumor being malignant is more or less inversely proportional to the size of the gland.
• usually occur in adults.
• with a slight female predominance. Warthin tumors occur much more often in males than in females, perhaps reflecting the historically higher prevalence of smoking, a predisposing factor, among men.
• The benign tumors most often appear in the fifth to seventh decades of life. The malignant ones tend to appear somewhat later.
• both benign and malignant lesions range from 4 to 6 cm in diameter and are mobile on palpation except in the case of neglected malignant tumors.

• Although benign tumors are known to have been present usually for many months to several years before coming to clinical attention, cancers are generally detected more quickly because of their rapid growth.

• Ultimately, however, there are no reliable clinical criteria to differentiate benign from malignant lesions.
<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
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<tbody>
<tr>
<td>Pleomorphic adenoma (50%)</td>
<td>Mucoepidermoid carcinoma (15%)</td>
</tr>
<tr>
<td>(mixed tumor)</td>
<td></td>
</tr>
<tr>
<td>Warthin tumor (5%-10%)</td>
<td>Adenocarcinoma (NOS) (10%)</td>
</tr>
<tr>
<td>Oncocytoma (1%)</td>
<td>Acinic cell carcinoma (5%)</td>
</tr>
<tr>
<td>Other adenomas (5%-10%)</td>
<td>Adenoid cystic carcinoma (5%)</td>
</tr>
<tr>
<td>Basal cell adenoma</td>
<td>Malignant mixed tumor (3%-5%)</td>
</tr>
<tr>
<td>Canalicular adenoma</td>
<td>Squamous cell carcinoma (1%)</td>
</tr>
<tr>
<td>Ductal papillomas</td>
<td>Other carcinomas (2%)</td>
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NOS, Not otherwise specified.
Pleomorphic Adenoma

- Mixed tumors.
- They represent about 60% of tumors in the parotid.
- **radiation** exposure increases the risk.
- chromosomal rearrangements involving PLAG1 (increase cell growth).
- These tumors present as painless, slow-growing, mobile, discrete masses within the parotid or submandibular areas or in the buccal cavity.
- The recurrence rate (perhaps months to years later) with parotidectomy is about 4% but, with simple enucleation approaches 25%.
• A carcinoma arising in a pleomorphic adenoma is referred to variously as a carcinoma ex pleomorphic adenoma or a malignant mixed tumor.

• The incidence of malignant transformation increases with time, being about 2% for tumors present less than 5 years and almost 10% for those present for more than 15 years.

• Malignant mixed tumors are among the most aggressive of all salivary gland malignant neoplasms, producing mortality rates of 30% to 50% at 5 years.
Figure 16-15 Pleomorphic adenoma. A, Slowly enlarging neoplasm in the parotid gland of many years duration. B, The bisected, sharply circumscribed, yellow-white tumor can be seen surrounded by normal salivary gland tissue.
Figure 16-16 Pleomorphic adenoma. A, Low-power view showing a well-demarcated tumor with adjacent normal salivary gland parenchyma. B, High-power view showing epithelial cells and myoepithelial cells within a chondroid matrix material.
Warthin Tumor

• Papillary Cystadenoma Lymphomatosum.
• the second most common salivary gland neoplasm.
• arises almost **exclusively** in the parotid gland.
• Occurs more commonly in males than in females, usually in the fifth to seventh decades of life.
• 10% are multifocal
• 10% bilateral.
• **Smokers** have eight times the risk of nonsmokers for developing these tumors.
• These neoplasms are benign, with recurrence rates of only 2% after resection.
Figure 16-17 Warthin tumor. A, Low-power view showing epithelial and lymphoid elements. Note the follicular germinal center beneath the epithelium. B, Cystic spaces separate lobules of neoplastic epithelium consisting of a double layer of eosinophilic epithelial cells based on a reactive lymphoid stroma.
Mucoepidermoid Carcinoma

- represent about 15% of all salivary gland tumors.
- while they occur mainly (60% to 70%) in the parotids, they account for a large fraction of salivary gland neoplasms in the other glands, particularly the minor salivary glands.
- The most common form of primary malignant tumor of the salivary glands.
- $t(11,19)$ ------------ MECT1 ,MAML2 genes
Figure 16-18  

A, Mucoepidermoid carcinoma growing in nests composed of squamous cells as well as clear vacuolated cells containing mucin. 

B, Mucicarmine stains the mucin reddish pink.
• The clinical course and prognosis depend on the grade of the neoplasm.

• **Low-grade tumors**: rarely do they metastasize and so yield a 5-year survival rate of more than 90%.

• **High-grade neoplasms**: are invasive and difficult to excise and so recur in about 25% to 30% of cases and, in 30% of cases, metastasize to distant sites. The 5-year survival rate in patients with these tumors is only 50%