

Oral Medicine

BENIGN, PREMALIGNANT, AND MALIGNANT LESIONS OF THE ORAL CAVITY

BENIGN SOFT TISSUE LESIONS

Oral mucosal benign tumors comprise lesions that form from epithelial, fibrous tissue, adipose tissue, nerve, and muscle. Benign proliferations of blood vessels and lymphatic vessels resemble neoplasms but do not have unlimited growth potential and therefore are more appropriately considered hamartomatous proliferations.

Epithelial Tumors

There are several benign oral epithelial virus-induced growths, principally those caused by the human papillomavirus (HPV).

Benign oral epithelial HPV-induced growths is called viral papilloma (also called squamous papilloma). It usually occurs in the third to fifth decades, most commonly as an isolated small growth (<1 cm diameter) on the palate,



ranging in color from pink to white, ridged or wrinkled exophytic, and pedunculated lesion. When these lesions occur on the surface of the lips, alveolar gingivae, or palate, they are well keratinized, while on nonkeratinized mucosal surfaces, they appear soft and pink/red. HPV is DNA virus detected in approximately 50% of squamous papillomas.

The common wart, verruca vulgaris, is generally found on the skin (sometimes in association with similar skin lesions, often on the fingers) and is caused by the cutaneous HPV subtypes 2 and 57. When involving the oral cavity, these warts are similar in appearance to viral papillomas and tend to involve the lips, gingivae, and hard palate. Oral papillomas and warts are clinically similar, and local excision is desirable. Care should be exercised when removing HPV-related oral lesions with electrocautery or laser as there exists the possibility of aerosolizing HPV particles. Although these lesions are probably infectious, a history of direct contact with another infected person is unusual, except in the case of multiple and often recurrent oral warts associated with sexual contact or maternal transmission, referred to as condyloma acuminatum

Keratoacanthoma; is a localized lesion that is typically found on sun-exposed skin, including the upper lip. The rapid growth of a keratoacanthoma may be quite frightening, to the point where it is often mistakenly diagnosed as squamous or basal

cell carcinoma. These lesions appear fixed to the surrounding tissue (similar to some carcinomas), often grow rapidly, and are usually capped by thick keratin. Occasionally, the lesion matures, exfoliates, and heals spontaneously, but more frequently, block excision is required, and the diagnosis is established from microscopic evaluation. Epithelial tissue adjacent to the lesion is sharply demarcated from that of the lesion, which appears to lie in a cup-shaped depression. The proliferating epithelium constituting this lesion consists of masses of reasonably well-differentiated squamous cells that often produce keratin pearls and show little cellular atypia. The lesion's usual location on the upper lip (where squamous cell carcinoma of actinic etiology is rare, compared with the lower lip) should remind the clinician to consider keratoacanthoma in the differential diagnosis. Intraoral keratoacanthomas are rare. Treatment of this lesion is conservative excision, although some believe that it is not clearly separable from squamous cell carcinoma and advocate wide excision to prevent recurrence.

Connective tissue lesions

Inflammatory/Reactive Hyperplasia of Soft Tissue; Wide range of commonly occurring exophytic or nodular growths of the oral mucosa is termed inflammatory hyperplasia.

The major etiologic factor for these lesions is generally assumed to be chronic trauma from ill-fitting dentures, calculus, overhanging dental restorations, acute or chronic tissue injury from biting, or fractured teeth. With some of these lesions (e.g., pregnancy epulis), the levels of circulating hormones play a role. The majority of lesions occur peripherally on the oral mucosal surface, where irritants are quite common and therefore are subject to continual masticatory trauma. Clinical appearance is swollen, distended, ulcerated, red to purple in color due to dilated blood vessels, and they exhibit acute and chronic inflammatory exudates and Erosion of the underlying cortical bone rarely occurs with peripheral inflammatory hyperplasias; if noted, there should be a strong suspicion that an aggressive process or even malignancy is involved.

Fibromas; may occur as either pedunculated or sessile (broadbased) growths on any surface of the oral mucous membrane.



They are also called traumatic or irritation fibromas. The majority remain small, and lesions that are >1 cm in diameter are rare. The giant cell fibroma exhibits a somewhat nodular surface and is histologically distinguished from other fibromas by

the presence of stellate shaped and multinucleated cells in the connective tissue. The etiology of the giant cell fibroma is not known.

Fibrous Inflammatory Hyperplasias

The epulis fissuratum is a reactive inflammatory lesion associated with the periphery of ill-fitting dentures that histologically resembles the fibroma. The growth is often split by the edge of the denture, resulting in a fissure, one part of the lesion lying under the denture and the other part lying between the lip or cheek and the outer denture surface.



This lesion may extend the full length of one side of the denture. Many such hyperplastic growths will become less edematous and inflamed following the removal of the associated chronic irritant, but they rarely resolve entirely. In the preparation of the mouth to receive dentures, these lesions are excised to prevent further irritation and to ensure a soft tissue seal for the denture periphery.

Pulp polyps or chronic hyperplastic pulpitis represents an analogous condition.



They occur when the pulpal connective tissue proliferates through a large pulpal exposure and fills the cavity in the tooth with a mushroom-shaped polyp that is connected by a stalk to the pulp chamber. Masticatory pressure may lead to keratinization of the epithelium covering these lesions. Pulp polyps contain few sensory nerve fibers and are remarkably insensitive. The crowns of teeth affected by pulp polyps are usually so badly destroyed by caries that endodontic treatment is not feasible.

Pyogenic Granuloma, Pregnancy Epulis, and Peripheral Ossifying or Cementifying Fibroma

Pyogenic granuloma is a hemorrhagic nodule that occurs most frequently on the gingiva (although it can occur on any surface) and that has a strong tendency to recur after simple excision if the associated irritant is not removed. It may be difficult on occasion to identify the causative chronic irritation for these lesions, but their proximity to the gingival margin suggests that calculus, food materials, and overhanging dental restoration margins are important irritants that should be eliminated when the lesion is excised.

Identical lesions with the same histologic structure occur in association with the florid gingivitis and periodontitis that may complicate pregnancy and are referred to as

pregnancy epulis or **pregnancy tumor**. The prevalence of pregnancy epulides increases toward the end of pregnancy (when levels of circulating estrogens are highest), and they tend to shrink after delivery (when there is a precipitous drop in circulating estrogens). This suggests that hormones play a role in the etiology of the lesion. Both pyogenic granulomas and pregnancy epulides may mature and become less vascular and more collagenous, gradually converting to fibrous epulides. Small isolated pregnancy tumors occurring in a mouth that is otherwise in excellent gingival health may sometimes be observed for resolution following delivery, but the size of the lesion or the presence of a generalized pregnancy gingivitis or periodontitis supports the need for treatment during pregnancy.



The peripheral ossifying or cementifying fibroma is found exclusively on the gingiva; it does not arise in other oral mucosal locations. Clinically, it varies from pale pink to cherry red and is typically located in the interdental papilla region. This reactive proliferation is named because of the histologic evidence of calcifications that are seen in the context of a hypercellular fibroblastic stroma. Peripheral ossifying or cementifying fibromas occur in teenagers and young adults and are more common in women. The existence of these lesions indicates the need for a periodontal consultation, and treatment should include the elimination of subgingival irritants and gingival pockets throughout the mouth, as well as excision of the gingival growth.

Peripheral Giant Cell Granuloma

Giant cell granuloma occurs either as a peripheral exophytic lesion found exclusively on the gingiva or as a centrally located lesion within the jaw, skull, or facial bones. Peripheral giant cell granulomas are five times as common as the central lesions. Both peripheral and central lesions are histologically similar and are considered to be examples of benign inflammatory hyperplasia in which cells with fibroblastic, osteoblastic, and osteoclastic potential predominate in the tissue.

Vascular Anomalies

Hemangiomas

Hemangiomas of the head and neck are true neoplasms and appear a few weeks after birth and grow rapidly. They have been described in almost all head and neck locations in a variety of presentations: superficial and deep, small and large, most commonly as solitary lesions but also as multiple lesions. Small lesions may be

clinically indistinguishable from pyogenic granulomas and superficial venous varicosities.



Care should be taken in performing biopsies or excising all vascular lesions:

- 1-they have a tendency for uncontrolled hemorrhage
- 2- The extent of the lesion is unknown since only a small portion may be evident in the mouth.

Lymphangioma

lymphatic malformation similar to other vascular malformations. It is characterized by an abnormal proliferation of lymphatic vessels. The most common extraoral and intraoral sites are the neck (predominantly in the posterior triangle) and tongue, respectively. The vast majority (80%–90%) of lymphangiomas arises within the first 2 years of life and are an important cause of congenital macroglossia. Clinically, lymphangiomas are a slow-growing and painless soft tissue masses. They may undergo a rapid increase in size secondary to inflammation from an infection or hemorrhage from trauma. Large lymphangiomas may become life threatening if they compromise the airway or vital blood vessels, and those spreading into and distending the neck are macrocystic and are referred to as cystic hygromas.

Differential diagnoses of lymphatic malformations of the tongue include infantile hemangioma or other vascular malformations, congenital hypothyroidism, mongolism, amyloidosis, neurofibromatosis, various storage diseases, and primary muscular hypertrophy of the tongue, all of which may cause macroglossia.

Neurogenic Lesions

Traumatic Neuroma

A traumatic neuroma is not a true tumor but a proliferation of nerve tissue that is caused by injury to a peripheral nerve. Nerve tissue is encased in a sheath composed of Schwann cells and their fibers. When this sheath is disrupted, the nerve loses its framework. When a nerve and its sheath are damaged, the proximal end of the damaged nerve proliferates into a mass of nerve and Schwann cells mixed with dense fibrous scar tissue. In the oral cavity, injury to a nerve may occur from injection of local anesthesia, surgery, or other sources of trauma. Traumatic neuromas are often painful. The discomfort may range from pain on palpation to severe and constant pain. Most traumatic neuromas occur in adults. Traumatic neuromas in the oral cavity may occur in any location where a nerve is damaged; the mental foramen area is the most common location. The definitive diagnosis is made on the basis of a biopsy and microscopic examination. Traumatic neuromas are treated by surgical excision. Recurrence rates for neuromas are rare.

Neurofibromatosis

Multiple neurofibromas occur in a genetically inherited disorder known as neurofibromatosis 1 (NF1) or von Recklinghausen's disease. This disease is transmitted as an autosomal dominant trait, and the *NF1* gene has been identified. Oral neurofibromas are a common feature of the disease. The presence of numerous neurofibromas or a plexiform-type neurofibroma is pathognomonic of NF1.

Patients with NF1 are at increased risk of the development of malignant tumors, especially malignant peripheral nerve sheath tumor, leukemia, and rhabdomyosarcoma

Lipoma

The lipoma is a benign tumor of mature fat cells. When occurring in the superficial soft tissue, the lipoma appears as a yellowish mass with a thin surface of epithelium. Because of this thin epithelium, a delicate pattern of blood vessels is usually observed on the surface. Deeper lesions may not demonstrate this finding and therefore are not as easily identified clinically. The majority of oral lipomas are found on the buccal mucosa and tongue and occur in individuals over 40 years of age, without any sex predilection. The lipoma is treated by conservative surgical excision and generally does not recur.

Tumors of Muscle

Tumors of muscle are extremely uncommon in the oral cavity. The rhabdomyoma, a benign tumor of striated muscle, has been reported to occur on the tongue. The vascular leiomyoma, a benign tumor of smooth muscle cell and vascular endothelium, occasionally occurs in the oral cavity. Treatment is local surgical excision, and recurrence is rare.

Premalignant and malignant lesions of the oral mucosa

1-Hyperkeratosis (focal keratosis) is a microscopic term meaning increased thickness of the keratin layer of stratified squamous epithelium with no microscopic evidence of atypical epithelial cells. Clinically, hyperkeratotic lesions appear as white, rough, non-painful patches that do not rub off. They are often secondary to chronic irritation, such as biting, tooth irritation, or tobacco use. Hyperkeratotic lesions on oral mucosal surfaces that are normally keratinized, such as dorsum of the tongue, hard palate, and attached gingiva, sometimes represent a physiologic response (callus) to chronic irritation. These lesions will usually resolve if the irritant is removed. Hyperkeratotic lesions on surfaces that are normally nonkeratinized are potentially more serious and should be biopsied if they do not resolve if irritants are removed. Remember, however, that dysplasia, carcinoma *in situ*, and squamous cell carcinoma can occur on any oral mucosal surface.

2-Epithelial dysplasia is atypical or abnormal growth of the stratified squamous epithelium lining a mucosal surface. It is a diagnosis that must be made microscopically. These lesions appear clinically as white, rough, non-painful areas, or non-painful red patches ("erythroplakia" or "erythroplasia"), or patches that demonstrate both red and white areas. Because these lesions are asymptomatic, the patient is usually not aware of them. Some lesions diagnosed as epithelial dysplasia

will progress to squamous cell carcinoma, while others will resolve. Since it is impossible to determine by microscopic examination which lesions will progress or resolve, treatment is complete surgical excision, if possible, and follow-up.

3-Carcinoma in situ is cancer of the oral epithelium which is confined to the epithelial layer. It presents most commonly as a persistent red plaque (erythroplakia) or a mixed white and red plaque. It may also appear as a white plaque. Complete removal is the treatment. When completely removed, the prognosis is excellent, although the patient is at increased risk of developing new lesions at other locations on the oral mucosa.

4-Squamous cell carcinoma is the most common malignant neoplasm of the oral cavity. Tobacco and alcohol use and human papilloma virus infection have been identified as risk factors, but squamous cell carcinoma can occur in patients with no known risk factors. Squamous cell carcinoma can occur anywhere on the oral mucosa, but is most common on the ventral and lateral surfaces of the tongue, floor of the mouth, soft palate, tonsillar pillar area, and retromolar trigone areas. Superficially invasive, or early, squamous cell carcinoma lesions appear as surface lesions rather than soft tissue enlargements. They are almost invariably non-painful, and thus patients do not know they have a lesion. Early lesions may be white rough epithelial thickening lesions, red persistent non-painful lesions, or a combination of the two. It is important to recognize squamous cell carcinoma in its early stages when cure is possible without disfiguring surgery. The main treatment for oral squamous cell carcinoma is complete surgical excision. Lymph node dissection is performed when lymph nodes are involved. Radiation therapy is often used as an adjunct to surgery. Chemotherapy is reserved for palliative therapy.

Oral and Oropharyngeal Cancer of the oral cavity and pharynx affects 10.8 of every 100,000 individuals in the United States, based on the National Cancer Institute data. In South and Southeast Asia, the prevalence of oral cancer is high. Oral cancer is ranked one of the sixth most frequent malignancies in Asia. Cultural habits, including betel quid chewing, alcohol consumption, and reverse smoking, as well as low socioeconomic status and low consumption of fruits and vegetables contribute to this high prevalence. The majority of oral cancers are squamous cell cancers. Other malignant diseases that can occur in the oral cavity include tumors of the salivary glands, lymph nodes, bone, and soft tissue. Approximately 95% of oral cancer occurs in people older than 40 years, with an average age at diagnosis of approximately 60 years.

The majority of oral cancers involve the lateral borders and base of the tongue. The lips, gingiva, dorsal tongue, palate, and salivary glands are less common sites. Primary squamous cell carcinoma (SCC) of bone is rare; however, a tumor may develop from epithelial rests and from epithelium of odontogenic lesions, including cysts and benign lesions.

Oral cancer is age related disease, which may reflect time for the accumulation of genetic changes and duration of exposure to initiators and promoters. These include chemical and physical irritants, viruses, and hormonal effects, In addition, decreased

immunologic surveillance over time. Tobacco products and alcohol are the risk factors for oral cancer. Nicotine is a powerful and addicting drug. Epidemiologic studies have reported that up to 80% of oral cancer patients were smokers. In addition to the risk of developing primary cancers, the risk of recurrent and second primary oral cancers is related to continuing smoking after cancer treatment. Alcohol, including, wine, and beer, have been implicated in the etiology of oral cancer. The combined effects of tobacco and alcohol result in a synergistic effect on the development of oral cancer which may include dehydrating effects of alcohol on the mucosa, increasing mucosal permeability, and the effects of potential carcinogens in alcohol or tobacco as well as influence central nervous system activity.

In addition, Betel (Areca) Nut, Human Papilloma Virus and nutritional factors are predisposing or precipitating factors.

Nutritional factors such as Consumption of fruits and vegetables which is associated with a reduced risk for oral cancer. This may be due to the antioxidant vitamins C and E and flavonoids. Vitamin A may play a protective role in oral cancer.

There is no evidence that denture use, denture irritation, irregular teeth or restorations, and chronic cheek-biting habits are related to oral cancer risk.

The WHO has listed several oral conditions as having the potential to transform into oral cancer, including lichen planus, leukoplakia, erythroplakia, actinic cheilitis, and submucous fibrosis. Under the term “leukoplakia,” proliferative verrucous leukoplakia is more aggressive and has a high risk of progression to SCC.

Presenting Signs and Symptoms

The high-risk sites for oral carcinoma include the lower lip, the anterior floor of the mouth, and the lateral borders of the tongue.

Discomfort is the most common symptom that leads a patient to seek care and may be present at the time of diagnosis in up to 85% of patients.

mass in the mouth or neck.

Dysphagia, and limited movement, oral bleeding, neck masses, and weight loss may occur with advanced disease.

Loss of sensory function,.

Loss of function involving the tongue can affect speech, swallowing, and diet.

Possible tissue changes may include a red, white, or mixed red-and-white lesion; a change in the surface texture producing a smooth, granular, rough, or crusted lesion; or the presence of a mass or ulceration.

Lymphatic spread of oral carcinoma most commonly involves the submandibular and digastric nodes, and the upper cervical nodes, but can also involve the remaining nodes of the cervical chain.

Staging of Oral Cancer—TNM System

The American Joint Committee on Cancer (AJCC) has developed Tumor-Nodes-Metastasis (TNM) staging system of cancer, which reflects the prognosis, and is therefore determinants for the treatment strategy.

T is the size of the primary tumor,

N indicates the presence of regional lymph nodes, and

M indicates distant metastasis.

The staging system for OSCC combines the T, N, and M to classify lesions as stages 1 through 4. The AJCC classification is principally a clinical description of the disease.

Stage grouping

Stage 0	Tis N0 M0
Stage I	T1 N0 M0
Stage II	T2 N0 M0
Stage III	T3 N0 M0
	T1 N1 M0
	T2 N1 M0
	T3 N1 M0

Treatment of oscc depends on

- cell type
- degree of differentiation,
- the site and size of the primary lesion
- lymph node status
- the presence of local bone involvement
- the ability to achieve adequate surgical margins
- the presence or absence of metastases

Surgery and radiation are used with curative intent in the treatment of oral cancer. Chemotherapy and targeted therapy are used together with the principal therapeutic modalities of radiation and surgery and is now considered the benchmark for management of advanced disease. Either surgery or radiation may be used for T1 and T2 lesions; however, combined radiation and chemotherapy with or without surgery is usually employed for more advanced disease.

Recently, Photodynamic therapy applies light over a tissue that initially absorbed exogenous sensitizer. The sensitizing agent may be delivered systemically or topically and then after it selectively accumulates in target tissue. The subsequent light delivery to the target tissue results in cellular destruction. Due to the focused cellular destruction, the complications and disfigurement associated with this treatment are relatively small.

Malignant Tumors of the Salivary Glands

Salivary gland tumors most commonly arise in the parotid glands, where the majority of tumors are benign. Malignant tumors of the salivary glands develop more commonly in the submandibular, sublingual, and minor salivary glands.

Malignant salivary gland tumors most commonly present as a painless mass. When the mass is superficial or large, it may cause intraoral or extraoral asymmetry. When the mass is intraoral, it may be ulcerated. Neurologic involvement may lead to discomfort and numbness, and with parotid gland tumors, involvement of the facial nerve may cause facial paralysis. In the floor of the mouth, the salivary gland cancer may cause ankyloglossia. The most common site of minor salivary gland cancer is the posterior hard palate, but other sites in the oral cavity or upper respiratory tract may be involved. Biopsy of masses in the major glands may be accomplished by FNA (fine needle aspirate). However, surgical biopsy may be necessary if FNA is not diagnostic.

Sarcomas of the Soft Tissues

Soft tissue sarcomas of the oral cavity are rare and account for approximately 1% of all oral malignancies. include fibrosarcoma, malignant fibrous histiocytoma,

liposarcoma, rhabdomyosarcoma, leiomyosarcoma, angiosarcoma, and alveolar soft part sarcoma. Soft tissue sarcoma usually presents as a slow- or rapid-growing swelling of the mucosa involving any part of the oral cavity. Treatment usually consists of surgery with adjuvant radiotherapy for those with high-grade tumors and/or positive margins following surgery.

The most common bone-originating jaw malignancy.

Osteosarcoma

Osteosarcoma is a malignant tumor, characterized by the formation of bone or osteoid by tumor cells. Osteosarcomas of the jaws may develop in a broad range of ages but are more common in the third and fourth decade. Osteosarcoma occurs slightly more often in the mandible than in the maxilla. Most osteosarcomas of the jaws are centrally located in the bone. Osteosarcomas may also develop in a patient affected by Paget's disease or in a patient who has been irradiated either for a benign bone lesion or for adjacent soft tissue disease.

The most common presenting finding of osteosarcomas of the jaws is mass. Pain, and trigeminal sensory disturbances accompanies the swelling. Additional symptoms associated with intraosseous location consist of mobile teeth, toothache, and nasal obstruction.

The radiographic appearance varies between radiopaque, radiolucent, and mixed. The border of the lesion is not well defined. The classic radiograph presentation of "sun ray appearance," in which the radiograph may show an opaque lesion, with bony trabeculae directed perpendicularly to the outer surface.

In the presence of teeth, a widening of the periodontal ligament may be observed even before changes can be noticed elsewhere in the bone. Root resorption may create a spiky shape to the apical third. Loss of follicular cortices of unerupted teeth is highly suggestive of malignancy. Widening of the mandibular canal is another ominous sign. Treatment requires aggressive local surgery and the use of adjuvant chemotherapy, chemotherapy did not dramatically alter the prognosis of osteosarcoma of the jaw.