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## Oral Cancers

### Key Points

1. Oral Cancers often present as advanced stage disease.
2. Survival is less than 50% for patients with advanced oral cancer.
3. Early diagnosis leads to better outcomes.
4. Squamous cell carcinoma is the most common oral malignancy.
5. The oral cavity and the oropharynx represent different anatomic sites and treatment for cancers of these areas differ.
6. Optimal management of patients with oral cancers involves a multidisciplinary team approach.
7. Predictable genetic alterations found in premalignant and malignant epithelium may lead to earlier detection and novel therapies in the future.

### Introduction

An estimated 29,370 cases of oral cancer will be diagnosed in the United States in 2005.<sup>1</sup> The incidence in women is increasing due to increased use of tobacco products. Unfortunately, many patients will present with advanced stage disease, and cure will be unlikely. Five year survival for patients who present with advanced oral cancer is less than 50%. Advanced stage disease often requires treatments resulting in severe functional and cosmetic impairment. On the other hand, oral cancer can be highly curable with minimal morbidity if diagnosed early and managed appropriately. Recognizing the signs and symptoms of oral cancer leads to better outcomes and longer survival for afflicted patients. The purpose of this article is to provide primary care physicians with a better understanding of the anatomy, biology, presenting signs and symptoms, staging, and treatment options for patients who develop oral cancers.

### Anatomy

The oral cavity includes all structures in the mouth from the lips to the posterior one third of the tongue and junction of the hard and soft palate. Anatomic subsites include the lips, teeth, gingiva, buccal mucosa, hard palate, floor of mouth and anterior two thirds of the tongue. The oropharynx includes the soft palate, tonsils, base of tongue and posterior pharyngeal wall. The circumvallate papillae, a “V-shaped” ridge of large taste buds at the back of the tongue form the anatomic boundary between the oral tongue and the pharyngeal tongue. Why is this important? Squamous cell carcinomas (SCC), by far the most common type of oral cancer, behave differently and have different functional outcomes as a result of treatment when they occur in the oral cavity versus the oropharynx.

### Diagnosis and Workup

As with any disease, the workup of head and neck tumors begins with a focused history and physical examination. Worrisome historical features include:

1. A sore that won't heal
2. Dentures that no longer fit well
3. Pain in the throat which radiates to the ear
4. Dysphagia
5. Dysarthria
6. Neck lump
7. Bleeding from the oral cavity
8. Voice change
9. Weight loss

There are several known risk factors for head and neck SCC, and these should be identified during the initial workup of a suspicious lesion. There is a dose dependent relationship between the use of tobacco, including cigars, chew and snuff, and the development of SCC.<sup>2</sup> Marijuana use has also been demonstrated as a risk factor. The combination of tobacco and

alcohol leads to a synergistic effect, dramatically increasing one's risk. Sun exposure is a risk factor for lip cancer, particularly the lower lip. Finally, the discovery of human papilloma virus in a large percentage of oropharyngeal cancers has led many investigators to postulate oral sex as a risk factor for cancers of this area.<sup>3</sup>

A complete head and neck physical exam is the next step in the workup of a suspicious lesion. An adequate light source, such as a mag light or other bright flashlight helps with this. Suspicious characteristics include friability and induration. Friability can be demonstrated by lightly scraping a lesion with a tongue depressor and observing for bleeding. Induration, a sign of possible infiltration, can be determined by careful palpation of the lesion. Lesions which are infiltrative tend to be "rock hard" and sometimes fixed with respect to surrounding structures. Pain is a somewhat variable finding. Numbness of the lower lip or tongue, suggesting invasion of the inferior alveolar or lingual nerves, is another ominous sign when a large oral cavity tumor is present. Dysarthria, such as a "hot potato" voice, can occur in the presence of a large lesion of the oropharynx. The neck should be carefully palpated. Metastatic nodes are often firm, large, nontender and located deep in the neck. Fixation of a neck mass is ominous. A suspicious oral lesion in combination with a neck mass is highly suggestive of malignancy.

All patients with suspicious head and neck lesions should be referred to a head and neck surgeon for further workup. If there is palpable neck disease at presentation, a CT scan of the neck with intravenous contrast facilitates the workup. With few exceptions, this is the preferred imaging modality used for staging and anatomical assessment of head and neck cancers. At the time of otolaryngology consultation a detailed history and physical exam, including fiberoptic evaluation of the pharynx and larynx, will occur. During the initial consultation, office biopsy of most head and neck lesions can be performed. On occasion, patients with head and neck tumors will need to go to the operating room for biopsy. Staging endoscopy can be performed at this time. This consists of direct laryngoscopy, esophagoscopy, and bronchoscopy when indicated. All patients with newly diagnosed head and neck SCC must have these areas examined prior to treatment because of the relatively high incidence of synchronous cancers in this population. The concept of field cancerization states that because most patients with head and neck SCC have significant exposure to tobacco and alcohol, all of the mucosa of the upper aerodigestive tract is at risk for malignant transformation. Studies have demonstrated that up

to 10% of patients with SCC of the head and neck will have a second SCC elsewhere in the upper aerodigestive tract.<sup>4</sup> Once cancer has been proven by biopsy, a CT scan of the chest will be ordered to rule out distant metastasis. On occasion, a hybrid PET-CT may be included in the workup.

## Staging

The staging of cancers of the oral cavity and oropharynx determines prognosis and treatment options. In general, cancers of these areas tend to present with advanced stage disease. Table 1 gives the specific criteria for TNM staging. In general, advanced disease requires multiple therapeutic modalities. The three most commonly used modalities include surgery, radiation therapy and chemotherapy. These will be discussed later in this article. Unfortunately, despite advances in surgical and radiation techniques, long-term survival for patients with advanced disease remains poor. Five year survival for patients with stage 3 disease is 40% and stage 4 is less than 30%. Fortunately, for early disease, the prognosis can be good, better than 70% and 80% for stage 2 and 1 disease respectively. Therefore, early detection remains the primary factor for long-term survival.

### Table 1. TNM definitions

The American Joint Committee on Cancer (AJCC) has designated staging by TNM classification.

#### PRIMARY TUMOR (T)

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma in situ
- T1: Tumor 2 cm or less in greatest dimension
- T2: Tumor more than 2 cm but not more than 4 cm in greatest dimension
- T3: Tumor more than 4 cm in greatest dimension
- T4: (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, ie, chin or nose
  - T4a: (oral cavity) Tumor invades adjacent structures (eg, through cortical bone, into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)
  - T4b: Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

[Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4.]

## REGIONAL LYMPH NODES (N)

- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
- N2: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
  - N2a: Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in dimension
  - N2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
  - N2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N3: Metastasis in a lymph node more than 6 cm in greatest dimension

In clinical evaluation, the actual size of the nodal mass should be measured and allowance should be made for intervening soft tissues. Most masses larger than 3 cm in diameter are not single nodes but are confluent nodes or tumors in soft tissues of the neck. There are three stages of clinically positive nodes: N1, N2, and N3. The use of subgroups a, b, and c is not required but recommended. Midline nodes are considered homolateral nodes.

## DISTANT METASTASIS (M)

- MX: Distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis

## AJCC STAGE GROUPINGS

### 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

### Stage IVA

- T4a, N0, M0
- T4a, N1, M0
- T1, N2, M0
- T2, N2, M0
- T3, N2, M0
- T4a, N2, M0

### Stage IVB

- Any T, N3, M0
- T4b, any N, M0

### Stage IVC

- Any T, any N, M1

## Tumor Types

While SCC is the most common cancer to appear in the oral cavity and oropharynx, other types of malignancy can occur and should be mentioned. While it is beyond the scope of this article to discuss the different approaches for each of these tumor types, each of these behaves differently and responds to different forms of treatment. Salivary malignancies include adenoid cystic carcinoma and mucoepidermoid carcinoma. Soft tissue tumors, including osteogenic carcinoma and rhabdomyosarcoma, occur as well. Lymphoma may occur in the tonsils and base of tongue and usually presents as a painless asymmetric swelling. Lethal midline granuloma is a T-cell neoplasm that can erode through the palate and nose. Metastatic disease should be considered, especially in patients with a history of breast or prostate cancer, or any other malignancy with a tendency to metastasize to bone.

## Treatment

Patients with biopsy proven cancers of the oral cavity and oropharynx should be presented in a multimodality head and neck tumor planning conference. Optimal management of these complicated patients requires a team approach consisting of a head and neck surgeon, radiation oncologist, medical oncologist, pathologist, radiologist, dentist, specialty nurse, social worker, plastic surgeon and speech pathologist.

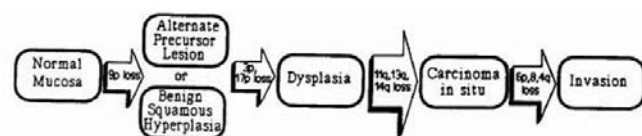
Three basic modalities exist for the treatment of head and neck SCC: surgery, external beam radiation therapy, and chemotherapy. In general SCC of the oral cavity is treated surgically, whereas SCC of the oropharynx is treated with radiation and chemo. Radical resection of oropharyngeal structures, such as the tongue base, leads to severe, disabling dysphagia and aspiration, often requiring permanent gastrostomy feeding as well as a tracheotomy. While this is considered highly controversial, many feel that “organ preservation” protocols involving chemo and/or radiation therapy lead to less severe functional consequences than surgery in the oropharynx and should therefore be the preferred treatment modality for this area of the head and neck.

The presence of the mandibular and maxillary bone makes delivery of an effective dose of radiation therapy difficult in the oral cavity. Tumors of the oral tongue, and floor of mouth, for example, are often better treated initially with surgery followed by radiation therapy if needed. Modern plastic surgical techniques make these areas more amenable to reconstruction. With the advent of microvascular free tissue transfer techniques in head and neck surgery, structures such as the mandible can be rebuilt using fibular bone-restoring cosmesis and preserving speech and deglutition. Large soft tissue defects may now be reconstructed with radial forearm free flaps, or rectus abdominis muscle. In addition, a variety of regional flaps may be used, giving the modern head and neck surgeon a large armamentarium of reconstructive choices.

### The Future

The field of cancer genetics holds the possibility of more effective, less disabling treatments for patients with advanced oral cancers. In recent years, the underlying genetic mechanisms of head and neck cancer have started to unravel. Califano, et al, recently published the Genetic Progression Model for head and neck cancer.<sup>5</sup> These findings demonstrated predictable genetic alterations that closely followed the progression of dysplastic oral epithelium to invasive SCC. See Figure 1 for a schematic of this. Reversal of these specific genetic alterations may one day lead to novel therapies and, hopefully, a cure for this type of cancer.

**Figure 1. Genetic Progression Model for Head and Neck Cancer**



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### CME Questions 5a-d

Please select the correct answer for the following:

- 5a. Squamous cell carcinoma is the most common type of oral cancer.
  - a. True
  - b. False
- 5b. The five-year survival rate for patients that present with advanced oral cancer is less than 50%.
  - a. True
  - b. False
- 5c. “Organ preservation” protocols, such as chemotherapy and/or radiation therapy, are the preferred treatment modalities in the treatment of cancers of the oropharynx.
  - a. True
  - b. False