

Empowering Physicians, Nurses and Other Non-Dental Healthcare Providers in the Prevention and Early Detection of Oral and Oropharyngeal Cancer

Susan Müller, DMD, MS, and Casey Hein, BSDH, MBA†*

**Approved for CME credit
(in Canada and the United States)**

Introduction

Oral cancer is the sixth-most common malignancy in the world. Statistics on the prognosis of oral and oropharyngeal cancer and survival rates provide a compelling rationale for enlisting non-dental healthcare providers (HCPs) in patient education and the prevention of oral cancer, and in the screening and referral of patients with suspicious lesions. Although oral cancer exams have traditionally been included in the scopes of practice of dentists and dental hygienists, the intervention of physicians, nurses and other non-dental HCPs offers great promise in reducing the incidence and sequelae of malignant lesions of the oral cavity.

This course provides information about oral and oropharyngeal cancer that is most relevant to physicians and other non-dental HCPs. It offers recommendations for effectively and efficiently incorporating into everyday patient care disease-management strategies that help ensure the timely identification of precancerous and cancerous lesions of the oral cavity and oropharynx. The clinical presentation and the signs and symptoms of potentially premalignant lesions in the oral cavity and oropharynx will be discussed and an overview of associated risk factors will be given. The course concludes by outlining important teaching points for educating patients at risk for oral and oropharyngeal cancer, and step-by-step directions to help patients perform a self-examination and to assist non-dental HCPs in performing a head and neck examination.

Keywords: *Oral cancer, oropharyngeal cancer, leukoplakia, erythroplakia, squamous cell carcinoma, mucositis*

*Professor, Department of Pathology and Laboratory Medicine, Department of Otolaryngology Head and Neck Surgery, Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA, United States. Email address: susan.muller@emoryhealthcare.org

†Assistant Professor, Division of Periodontics, Director of Education, International Centre for Oral-Systemic Health, Faculty of Dentistry; Assistant Professor, Director of Interprofessional Continuing Development, Division of Continuing Professional Development, Faculties of Medicine and Dentistry; University of Manitoba, Winnipeg, MB, Canada. Email address: casey.hein@med.umanitoba.ca

Learning Objectives

Upon completion of this course, participants will be able to:

1. Discuss the incidence of oral and oropharyngeal cancer.
2. Articulate the importance of early detection of oral and oropharyngeal cancer in overall survival rates, and obtaining a definitive diagnosis for oral lesions that persist for more than two weeks.
3. Identify lesions within the mouth and other clinical findings that may be precursors to oral and oropharyngeal cancer.
4. Identify the warning signs and symptoms of oral and oropharyngeal cancer.
5. Identify the risk factors associated with oral and oropharyngeal cancer that may help isolate behaviours and/or environmental exposures that place patients at greater risk.
6. Provide key information to educate at-risk patients about the prevention of oral and oropharyngeal cancer, and train patients how to perform an oral cancer self-examination.
7. Perform a head and neck examination to screen patients for potentially premalignant and malignant lesions, and make timely referrals to appropriate HCPs of patients with suspicious lesions.

Continuing Education Credit

This continuing education activity was developed under the auspices of the Division of Continuing Professional Development, Faculties of Medicine and Dentistry, University of Manitoba. Upon successful completion (80% pass rate), participants will be provided confirmation of educational credit.

RCPC Section 3 Credit

This activity is an Accredited Self-Assessment Program (Section 3) as defined by the Maintenance of Certification Program of The Royal College of Physicians and Surgeons of Canada, approved by the University of Manitoba's Division of Continuing Professional Development on May 1, 2013, and expires on April 30, 2016. Remember to visit MAINPORT (<https://mainport.royalcollege.ca>) to record your learning and outcomes. You may claim a maximum of 2 hours.

CFPC Mainpro–M1 Credit

This program meets the accreditation criteria of The College of Family Physicians of Canada and has been accredited by the University of Manitoba's Division of Continuing Professional Development for up to 2 Mainpro-M1 credits.

AMA PRA Category 1 Credit

Through an agreement between the American Medical Association and the Royal College of Physicians and Surgeons of Canada, the University of Manitoba's Division of Continuing Professional Development designates this activity for a maximum of 2 American Medical Association Physician's Recognition Award (AMA PRA) Category 1 credits. Physicians should only claim the credit commensurate with the extent of their participation in the activity.

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Scientific investigation conducted over the last several decades has provided compelling evidence that diseases and conditions of the oral cavity can have a profound and pervasive impact on overall health, especially in high-risk populations where access to care may be limited. With this emerging body of knowledge has come increased awareness that among non-dental healthcare providers (e.g., physicians, nurses, pharmacists and the greater allied healthcare community) there is a significant gap in knowledge about the interrelationships between oral and systemic health, or recognition of the significance of oral health in achieving and sustaining general health outcomes.

With appropriate education and training, physicians, nurses, pharmacists, dieticians, speech pathologists and other non-dental healthcare providers can significantly affect the epidemiologic trends in serious and often debilitating oral diseases and conditions. This innovative curriculum is the first comprehensive plan to fill the gaps in oral health knowledge and its application to practice in medicine, nursing and other healthcare disciplines.

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Case Study 1: Case in Point

This case study demonstrates a lost opportunity to identify a suspicious oral lesion and, subsequently, make a timely diagnosis and initiate treatment of oral cancer. This oversight is the result of a primary care provider (PCP) underestimating the malignant potential of a lesion of the tongue, which often occurs with younger patients. Unfortunately, cases like this are common.

Day 1: A 35-year-old female presented to her PCP, complaining of a tender area on the lateral border of her tongue. The patient was a non-smoker and drank alcohol occasionally. She had good oral care. The patient reported that she had had a sore throat prior to her tongue symptoms. On examination, a 1-cm area with both a red and white component was observed. The PCP placed the patient on an antibiotic for 10 days. (Figure 1 shows an example of a typical clinical manifestation of an initial lesion of squamous cell carcinoma of the tongue.)

Day 30: The patient returned 29 days later and reported that the antibiotic had initially worked but that the soreness had returned. Because of the recent antibiotic use, the PCP thought this represented oral candidiasis, and prescribed a two-week course of Nystatin (Mycostatin®).

Day 45: Fifteen days later, the patient called the PCP's office and reported that her symptoms had not improved. At this point, the physician prescribed two more weeks of Nystatin and asked the patient to return in two weeks for follow-up.

Day 60: The PCP re-examined the patient's tongue and found an ulcer, along with patches of red and white. The patient complained of increased pain and worried that she might be biting her tongue. The PCP referred the patient to her dentist. (Figure 2 shows an example of a typical clinical manifestation of an intermediate lesion of squamous cell carcinoma of the tongue.)

Day 70: When the patient's dentist evaluated the lesion, he noted a 1.5-cm ulcerated area with both a red and white component. On palpation, the area was firm. The dentist suggested smoothing the adjacent teeth in case this was causing the ulceration. The dentist also suggested that the patient change toothpaste and discontinue chewing cinnamon gum.

Day 84: After a two-week vacation, the patient returned to her dentist and reported that her symptoms had become progressively worse. The pain kept her up at night and she felt her tongue was swollen. The dentist noted that the area had grown larger, now measuring more than 2 cm with a 1-cm ulcer centrally located. The dentist referred the patient for a biopsy. (Figure 3 shows an example of a typical clinical manifestation of an advanced lesion of the tongue.)

Day 90: Approximately three months after the initial visit to her PCP, the patient had a biopsy, which confirmed squamous cell carcinoma. The biopsy and diagnosis were long overdue, demonstrating that even young, non-smoking patients can get oral cancer. The lesion was initially a stage T1, which could have required surgery alone. However, by this time, the lesion was a stage T2 tumour, which required a lymph node neck dissection and radiation. Consequently, this young patient's five-year survival rate decreased.



Figure 1. A typical clinical manifestation of an initial lesion of squamous cell carcinoma of the tongue.



Figure 2. A typical clinical manifestation of an intermediate lesion of squamous cell carcinoma of the tongue.



Figure 3. A typical clinical manifestation of an advanced lesion of squamous cell carcinoma of the tongue.

The Incidence of Oral and Oropharyngeal Cancer

Cancer of the oral cavity and oropharynx (combined) is the sixth-most common cancer in the world.¹ In 2010, there were 275,000 cases of oral cancer diagnosed worldwide. This accounts for 2% of all new cancer cases reported.² In the same year, 143,036 cases (worldwide) of oropharyngeal cancer were diagnosed.² Figure 4a shows the incidence of oral and oropharyngeal cancer in men, in countries that conduct surveillance; Figure 4b shows the incidence for women. It is clear that incidence and mortality rates are higher in men than in women. A country's distinct risk profile, as well as its availability and accessibility of health services, may account for these differences.

Oral cancer is the ninth-most common cancer in Canadian men, and it is estimated that 1,150 Canadians will die of the disease each year.³ The Canadian Cancer Society estimated that 2,700 men and 1,350 women would develop oral cancer in 2012.³

The American Cancer Society estimated that in the United States, 40,250 cases of oral and oropharyngeal cancer would be diagnosed in 2012, with associated deaths estimated at 8,000 men and women.⁴ The highest incidence of oral cancer is in Southeast Asia, with an incidence rate in men of 12.6 cases per 100,000 population. However, in most developed countries, the incidence rate in men is 1 to 10 cases per 100,000 population.²

In the United States, cancer of the lip, floor of the mouth, **buccal mucosa** and gingiva decreased in incidence between 1975 and 2009; however, a sharp increase in the incidence of tongue cancer and oropharyngeal cancer occurred during the same time period (see Figures 5 and 6).⁴ This trend has also been observed in Canada.⁵ Between 1992 and 2007, oropharyngeal tumours increased by 1.5% in men and 0.8% in women in the

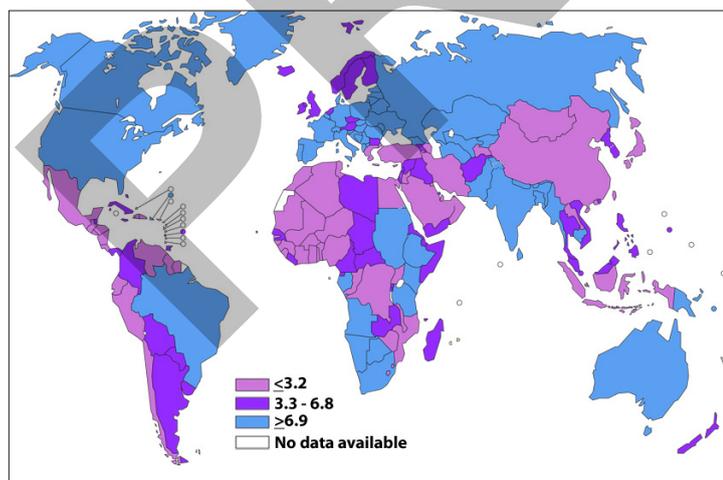


Figure 4a. Incidence of oral cavity cancer in men (ICD-10: C00–C08), age-standardized rate (ASR) per 100,000 world standard population, male (all ages). Source: GLOBOCAN 2002 International Agency for Research on Cancer, <http://www.depdb.iarc.fr/globocan/globocan2002.htm>.



Pearls to Practice

The Incidence of Oral and Oropharyngeal Cancer

1. There are a number of countries where the incidence of oral and oropharyngeal cancer is 6.9% or higher. For men, this higher incidence has been reported in Canada, the United States, Greenland, Australia, Brazil, Russia, India, Pakistan, Thailand and many countries in Europe and Africa. For women, this higher incidence has been reported in India, Pakistan and several countries in Africa. **HCPs in these countries should be aware of these epidemiologic statistics and carefully screen patients who may be at risk.**
2. Research on epidemiologic trends suggests a sharp increase in cancers of the tongue and oropharynx in Canada, the United States and certain European countries. Consequently, **HCPs in these countries should carefully screen their patients, especially men, for cancer of these subsites.**

United States, whereas oral cavity cancer decreased (2.3% in men, 0.4% in women).⁵ This trend has also been noted in other countries, including Scotland, Denmark, France and Germany.^{2,5,6}

The Importance of Early Detection of Oral and Oropharyngeal Cancer

Before we look at the various types of oral cancer, it is important to define several terms. According to the American Joint

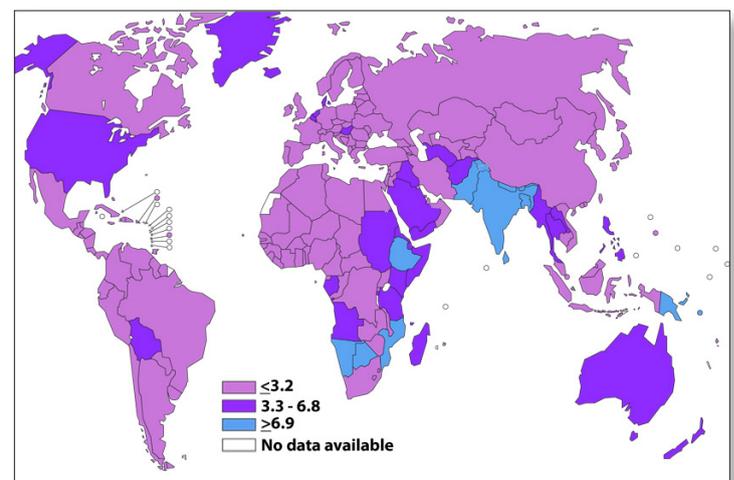


Figure 4b. Incidence of oral cavity cancer in women (ICD-10: C00–C08), age-standardized rate (ASR) per 100,000 world standard population, female (all ages). Source: GLOBOCAN 2002 International Agency for Research on Cancer, <http://www.depdb.iarc.fr/globocan/globocan2002.htm>.

Committee on Cancer (AJCC), the oral cavity begins at the junction of the cutaneous-vermilion border and extends to the junction of the hard and soft palate and to the line of the **circumvallate papillae** of the tongue (see Figure 7). These terms are also used by the International Union Against Cancer (UICC).⁷ The subsites of the oral cavity are further divided into the lip mucosa, buccal mucosa, lower and upper **alveolar ridge**, floor of the mouth, hard palate, anterior two-thirds of the tongue (also called the oral tongue) and the **retromolar trigone** (see Figure 8). The oropharynx extends from the junction of the hard and soft palate superiorly and to the hyoid bone inferiorly. The posterior one-third of the tongue (base of the tongue), the soft palate and uvula, the **palatine tonsils** and the lateral and posterior pharyngeal walls make up the oropharynx (see Figure 9).

More than 90% of malignancies occurring in the oral region are **squamous cell carcinoma (SCC or SqCC)** arising from the mucosal surfaces lining the oral cavity and the vermilion border of the lip.¹ Other cancers can occur in this region as well, especially salivary gland malignancies that arise from

the major salivary glands (see Figure 10): parotid, submandibular, sublingual and minor mucous glands found throughout the upper **aerodigestive tract**. Other malignancies do occur in the oral cavity region, but they are extremely rare. **Lymphomas, sarcomas, melanomas** and metastases to the oral cavity from other sites, including the lung, breast, prostate and colon, have been well documented⁸ (see Figure 11).

Unfortunately, the overall five-year survival rates of 50% for cancers of the tongue, oral cavity and oropharynx have not shown significant improvement in the past three decades. The five-year survival rate of lip cancer, at 90%, has a more favourable prognosis.

Both the AJCC and UICC use the staging of cancer to provide invaluable information to surgeons, oncologists and pathologists. The term "TNM" is used to describe the size of the cancer and whether or not it has extended to surrounding lymph nodes or has spread to distant sites, otherwise known as staging. TNM refers to the three main factors that are used to evaluate cancer stage: T for tumour size; N for lymph node involvement; and M for the presence of

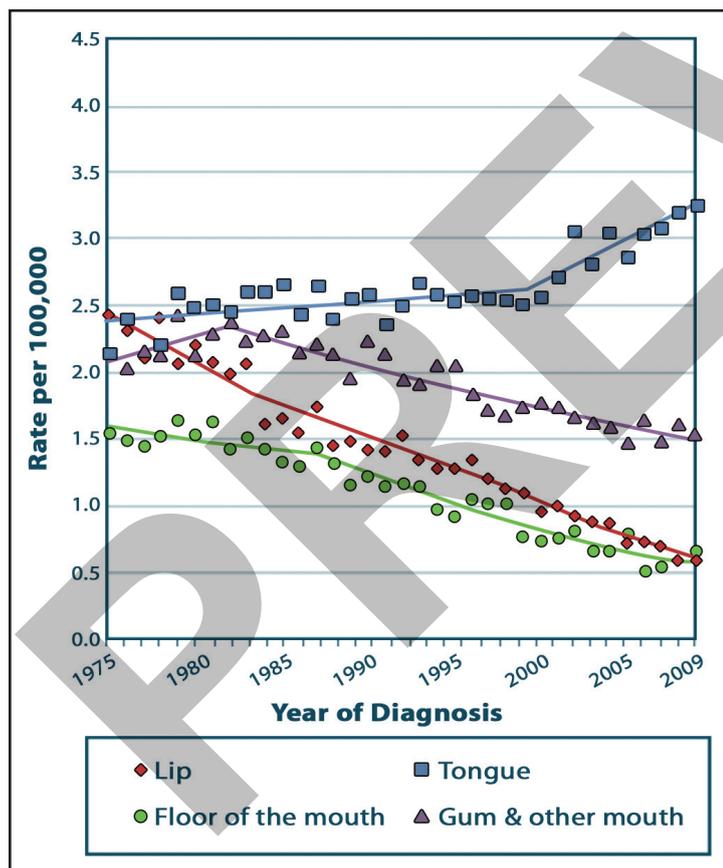


Figure 5. Age-adjusted SEER (Surveillance Epidemiology and End Rates) incidence rates by cancer site, all ages, all races, both sexes, 1975–2009 (SEER 9). Cancer sites include invasive cases only, unless otherwise noted. Incidence source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah and Atlanta). Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups—Census P25–1130). Regression lines are calculated using the Jointpoint Regression Program Version 2.5, April 2011, National Cancer Institute.

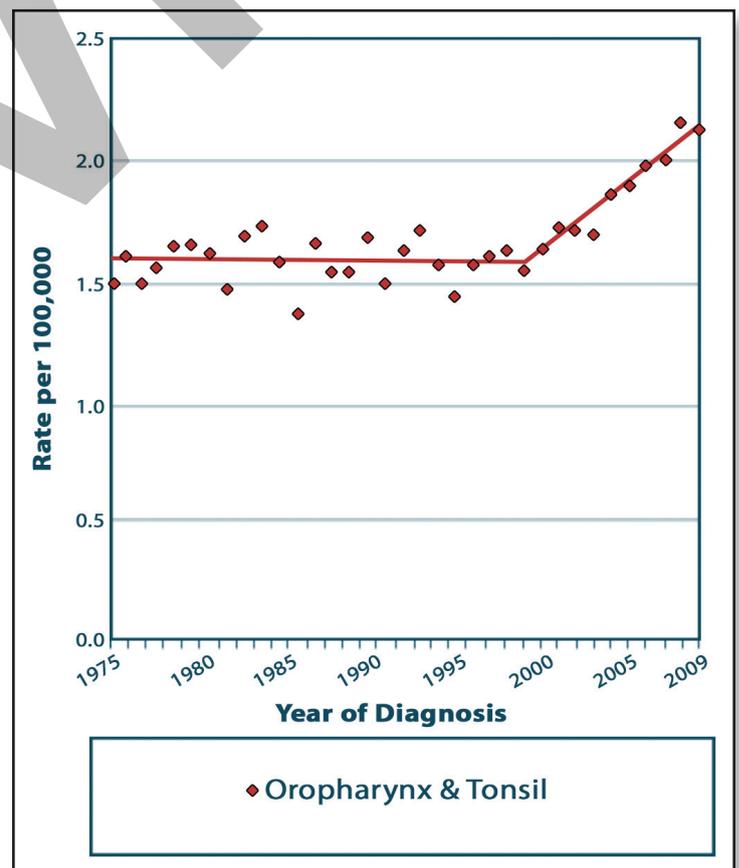


Figure 6. Age-adjusted SEER incidence rates by cancer site, all ages, all races, both sexes, 1975–2009 (SEER 9). Cancer sites include invasive cases only, unless otherwise noted. Incidence source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah and Atlanta). Rates are per 100,000 and are age-adjusted to the 2000 US Std Population (19 age groups—Census P25–1130). Regression lines are calculated using the Jointpoint Regression Program Version 2.5, April 2011, National Cancer Institute.

metastasis⁷ (see Table 1). TNM stage at presentation is an important predictor for prognosis.

In the advanced stage of oral cancer, treatments such as surgical intervention, chemotherapy and/or radiation treatment are associated with increased morbidity. This includes facial deformity and the impairment of speech, eating, drinking and swallowing. The five-year survival rate for oral cancers diagnosed early is 75%, compared to 20% for oral cancers diagnosed late. Clearly, early detection is critical not only for improving the overall survival rates from this deadly disease, but also for decreasing morbidity rates due to treatment. (Threats to overall health as a result of complications associated with the treatment of head and neck cancer are discussed extensively in another course within this curriculum, “Interprofessional Care of the Oral Cavity of Immunocompromised Patients.”)

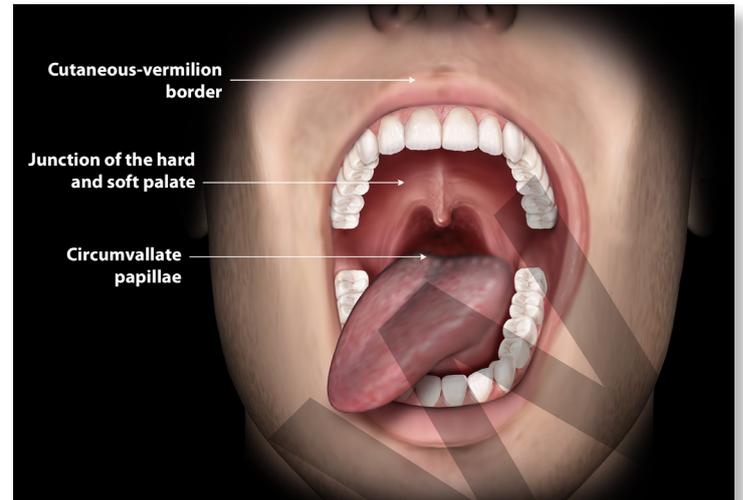


Figure 7. The oral cavity begins at the cutaneous-vermilion border and extends to the junction of the hard and soft palate and to the line of the circumvallate papillae of the tongue.

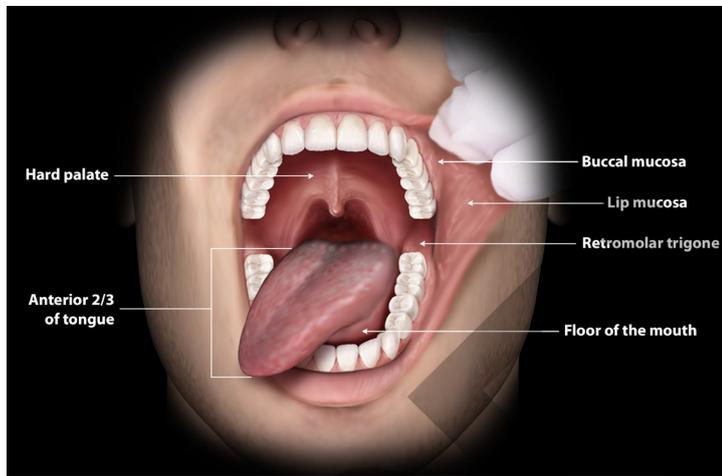


Figure 8. Subsites of the oral cavity, including the alveolar ridges.

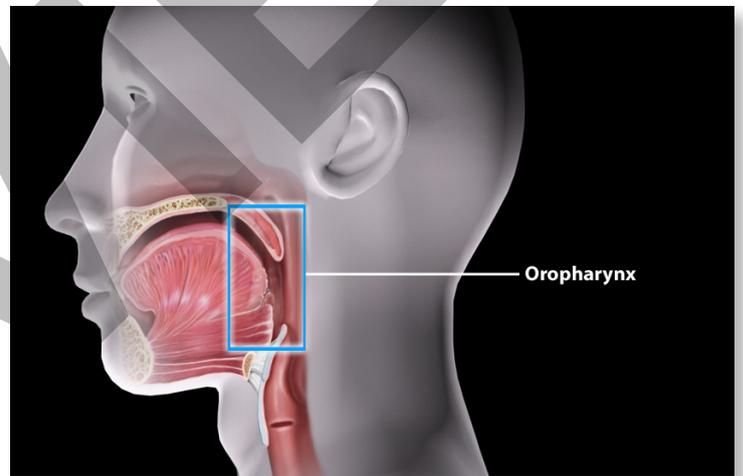


Figure 9. The oropharynx extends from the juncture of the hard and soft palate down to the lateral and posterior pharyngeal walls.

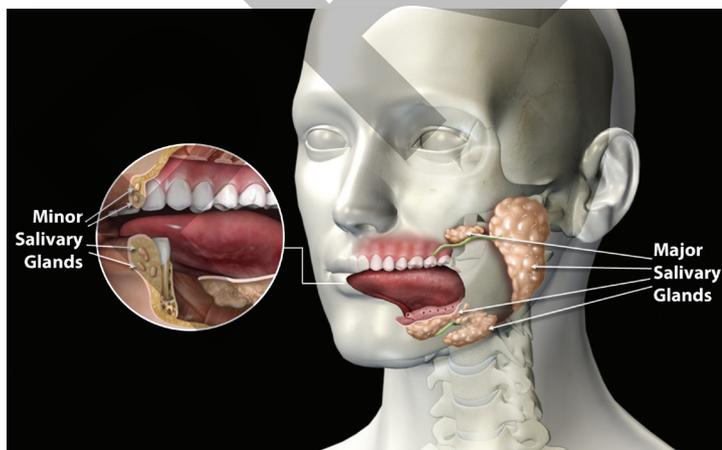


Figure 10. Locations of salivary gland malignancies.

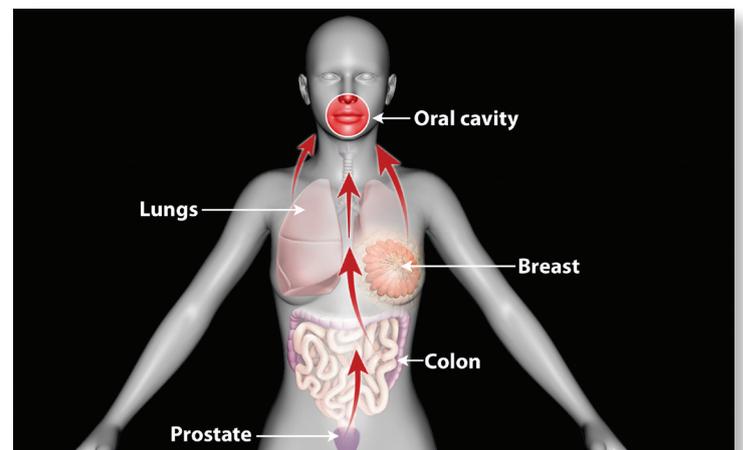


Figure 11. Anatomical sites from which cancer can metastasize to the oral cavity.



Pearls to Practice

The Importance of Early Detection of Oral and Oropharyngeal Cancer

1. More than 90% of malignancies of the mouth are squamous cell carcinomas on the mucosal surfaces lining the oral cavity and the vermillion border of the lip. **Therefore, HCPs should retract patients' cheeks and examine the vermillion border of the lip to identify suspicious mucosal lesions.**
2. **HCPs who treat patients with cancer of the lung, breast, prostate or colon should be aware of the potential for metastases to the oral cavity,** and carefully examine patients with cancer for suspicious oral lesions.
3. The five-year survival rate for oral cancers diagnosed early is 75%, compared to just 20% for oral cancers diagnosed late. **By incorporating oral cancer screening into routine physical examinations, non-dental HCPs can detect suspicious lesions at an early stage,** which will improve patients' overall survival rates.

Lesions and Other Clinical Findings as Potential Precursors to Oral and Oropharyngeal Cancer

Oral precancer is defined as morphologically and/or molecularly altered mucosa in which cancer is more likely to occur when compared to normal unaffected mucosa. The development of oral precancerous lesions is most likely multifactorial, and predicting which lesions will progress to squamous cell carcinoma is difficult. Two well-described precancerous (or potentially premalignant) lesions of the oral cavity are leukoplakia (see Figure 12) and erythroplakia (see Figure 13). Several other lesions identified as precancerous include actinic cheilitis (see Figure 14), oral submucous fibrosis (see Figure 15), smokeless tobacco keratosis (see Figure 16) and oral lichen planus (see Figure 17). Oropharyngeal cancer will also be discussed.

It is important to understand that not all dysplastic lesions progress to oral cancer, and that the grade of epithelial dysplasia does not correspond to risk for the development of oral cancer. In fact, some oral squamous cell cancers arise *de novo*, with no precursor lesion.

Oral Leukoplakia

The World Health Organization (WHO) defines oral leukoplakia as a white plaque or patch that cannot be rubbed

Table 1. Staging of Oral Cavity Tumours Based on American Joint Committee on Cancer

Stage at Diagnosis	5-Year Survival Rate				
	Overall	Lip	Tongue	Floor of the Mouth	Oropharynx
Stage 1: Localized to primary site Tumour ≤2 cm	82.5	96.3	70.0	72.5	56.0
Stage 2: Localized to primary site Tumour >2 cm and ≤4 cm	75.0	82.7	58.6	60.1	58.3
Stage 3: Localized to primary site Tumour >4 cm OR Any size primary tumour with a single <3 cm ipsilateral LN met	49%	56.7	47.3	35.8	55.8
Stage 4A: Any tumour size with a >3 cm but ≤6 cm ipsilateral LN OR Mets in multiple LNs, either ipsilateral or contralateral, none >6 cm OR Tumour with advanced local disease*	34.0	48.1	36.7	29.7	43.8
Stage 4B: Any tumour size with >6 cm LN OR Tumour with advanced local disease with any LN involvement Stage 4C: Any tumour with known distant metastases					

Abbreviations: LN: lymph node; met: metastases; *Tumour invades through adjacent structures: cortical bone, skin, extrinsic tongue muscles
Data source: National Cancer Institute SEER database 1988-2001; seer.cancer.gov

or scraped off and cannot be characterized as any other known disease or disorder.⁹ Other common white lesions in the mouth that can mimic oral leukoplakia include frictional keratosis, such as tongue and cheek biting (see Figures 18 and 19); lichenoid lesions (see Figure 20); lichen planus (see Figure 17); oral hairy leukoplakia (see Figure

21); hyperplastic candidiasis (see Figure 22); and tobacco pouch keratosis (see Figure 16).

Leukoplakia is a clinical term and does not predict oral cancer development. Accordingly, an international working group has suggested using the term “potentially malignant,” rather



Figure 12. Oral leukoplakia occurring on the ventral tongue. A biopsy of this lesion did not show dysplasia.

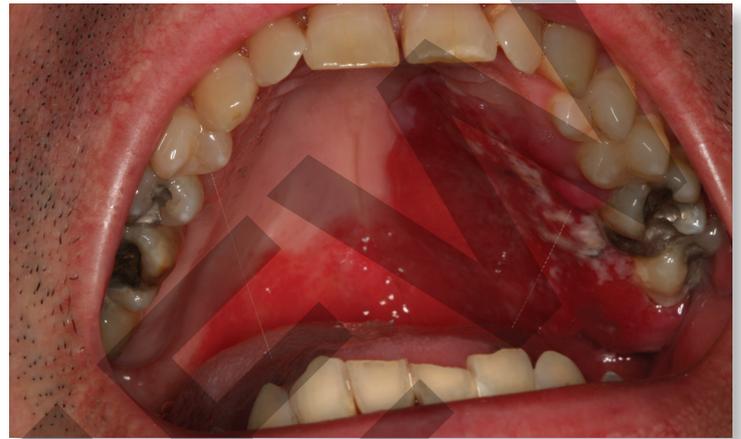


Figure 13. Erythroplakia of the palate. The lesion is well demarcated with a velvety texture. A biopsy was positive for squamous cell carcinoma.



Figure 14. Actinic cheilitis in a patient with a long history of sun exposure. There is blurring of the vermilion border and mottling of the lip mucosa. A biopsy showed mild dysplasia.

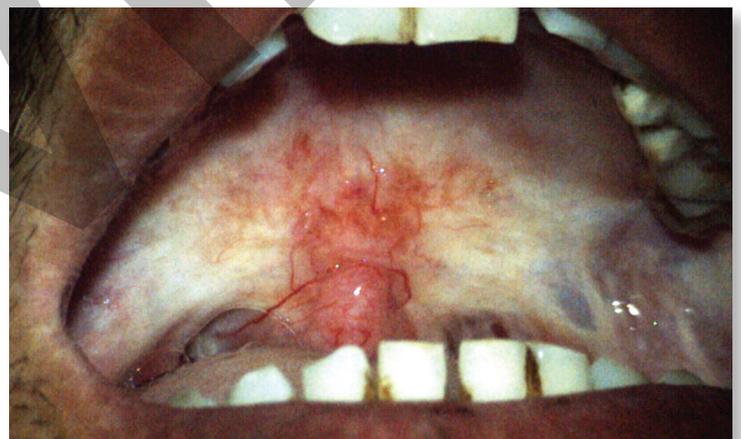


Figure 15. Submucous fibrosis in a South-Asian patient with a long history of betel nut use. The right and left palate show marked fibrosis appearing as pale pink to white tissue. Normal soft palate mucosa with red vasculature is seen on the midline



Figure 16. Anterior mandibular vestibule with an area of keratosis where smokeless tobacco is placed. A biopsy showed keratosis without dysplasia.



Figure 17. Oral lichen planus of the lateral tongue. There is a pattern of lace-like reticulations extending to the dorsal tongue. Oral lichen planus always affects more than one oral site. A biopsy confirmed the clinical diagnosis of lichen planus.



Figure 18. An area of frictional keratosis on the lateral border of the tongue caused by biting. A biopsy confirmed benign keratosis.



Figure 19. An area of keratosis on the buccal mucosa caused by a cheek biting and sucking habit. A biopsy confirmed benign keratosis.



Figure 21. Oral hairy leukoplakia presenting in a 54-year-old woman with HIV, with recent white plaques occurring bilaterally on the lateral and ventral tongue. A biopsy was positive for Epstein-Barr virus, and a diagnosis of oral hairy leukoplakia was confirmed.

than “precancerous,” when describing leukoplakia and possible oral cancer development.¹⁰ Figure 23 shows the various clinical appearances of leukoplakia, with an overview of the histologic changes that occur during the phases to malignant transformation.

Most cases of leukoplakia are identified in the fifth to seventh decades of life, with a greater incidence in men than women.^{10,11} Oral leukoplakia is an unusual finding in people younger than 30 years of age.¹¹ There are also wide geographic differences in the incidence of leukoplakia, ranging from 0.4% to 11.7%.¹² These reported variations are most likely due to cultural differences in diets, and in alcohol and tobacco habits (including the use, in some countries, of pan/betel quid). North American and European studies report the prevalence of oral leukoplakia at 2.0%, a rate that has remained relatively stable for the past 30–40 years.¹²

Although the premalignant potential of oral leukoplakia has been recognized since the mid-nineteenth century, predicting



Figure 20. Lichenoid reaction to a nonsteroidal medication. A large ulcer is noted, and, anterior to the ulcer, white striae mimicking lichen planus are seen. A biopsy showed a non-specific ulcer that lacked the features of lichen planus.



Figure 22. Hyperplastic candidiasis of the palate in a patient who recently took antibiotics for bronchitis. Unlike leukoplakia, the white plaques scrape off with a tongue blade. Microscopic examination of the scraped plaques confirmed the diagnosis of candidiasis.