Oral Cancer Risk and Detection: The Importance of Screening Technology

A Peer-Reviewed Publication
Written by Denis P. Lynch, D.D.S., Ph.D.

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Educational Objectives
Upon completion of this course, the clinician will be able to do the following:
1. Know the incidence of oral cancer in the United States and understand the risk factors
2. Be knowledgeable about the signs and symptoms of oral cancer
3. Understand screening methods available for the detection of oral cancer
4. Understand the role of chromosomal aberrations in the risk of malignant transformation

Abstract
In the United States in 2007, over 34,000 new cases of oral cavity and oropharyngeal cancer will be diagnosed. The single greatest risk factor for oral cancer in the United States is the use of tobacco. A strong association has been found between oral and oropharyngeal cancer and the presence of HPV in oral tissues. The five-year relative survival rate is estimated at 59.1% overall for oral and pharyngeal cancers diagnosed during 1996–2003. An estimated 85% of oral premalignant and malignant lesions present clinically as leukoplakias. Early detection of oral cancer is complicated by the fact that many lesions in their earlier stages may be completely asymptomatic, and the detection of suspicious lesions is increased through regular screening of patients. Historically, unaided visual examination, palpation, and radiographs were available for oral cancer screening. In recent years, screening technologies have become available that supplement the visual examination. If suspicious lesions are found during the screening procedure, the lesion must be biopsied or the patient referred to a specialist for further evaluation. The ability to identify lesions and to predict which lesions will undergo malignant transformation would facilitate early diagnosis and subsequent disease management tailored to the individual patient. The ultimate goals are to reduce both mortality and morbidity, and to improve patients’ quality of life.

Introduction/Overview
In the United States in 2007, over 34,000 new cases of oral cavity and oropharyngeal cancer will be diagnosed. During the same time period, over 7,000 affected individuals will die of these cancers.1 Worldwide, oral cancer accounts for 2%–4% of all cancer diagnoses. In some regions, the prevalence of oral cancer is much higher, representing approximately 10% of all cancers in Pakistan, and around 45% in the Indian subcontinent as a whole.2,3 The anatomic site of oral cancers also varies by geographic region. In the United States, the most common sites for oral cancer are the tongue and lip (Table 1).

Risk Factors
The single greatest risk factor for oral cancer in the United States is the use of tobacco, with combustible and smokeless tobacco being associated with 75% of all cases of oral cancer. Tobacco smoking carries a six-fold risk of developing oral cancer compared to not smoking. Smokeless (chewed) tobacco carries a significantly higher risk of oral cancer of the cheeks, inner lips and gingivae.4 Oral cancer is also six times more likely to develop in alcohol drinkers than in non-drinkers. The combination of tobacco use and alcohol abuse is particularly hazardous, posing a fifteen-fold risk of oral cancer for users compared to non-users.5 Lip exposure to ultraviolet radiation and HIV seropositivity are additional risk factors (Table 2). While tobacco and alcohol use are traditionally the greatest risk factors, it is important to consider other known risk factors, such as betel quid chewing, in certain ethnic populations. Betel quid chewing, prevalent for example in Asian Indian and Taiwanese populations, is associated with a significantly increased risk of oral cancer.6,7,8 The use of areca nut, narcotics or cannabis has also been found to be a risk factor for oral cancer.9 Given the multiethnic nature of the United States population, these risk factors must be considered in addition to tobacco use and ethanol consumption. Other factors associated with increased oral cancer risk include male gender, increasing age, genetic factors, and socioeconomic status. A reduced risk of oral cancer has been associated with a high dietary fruit and vegetable intake.10

The presence of certain human papillomaviruses (HPVs) is associated with a high lifetime number of sexual
partners. A strong association has been found between oral and oropharyngeal cancer and the presence of HPV in oral tissues, independent of smoking or drinking habits.11,12, 13 Specifically HPV-16 is considered an independent risk factor for oral and oropharyngeal cancer.14 One study of 143 patients found HPV-16 present in 16.8% of head and neck squamous cell carcinomas.15

**Morbidity and mortality**

Oral cancer is associated with significant morbidity and mortality. The five-year relative survival rate for oral and pharyngeal cancer is estimated at 59.1% overall for cases diagnosed during 1996–2003, up only slightly from the 1970s when the five-year relative survival rate was approximately 53%.16 By comparison, the five-year relative survival rate for breast cancer is currently 89%. Survival rates vary with the stage of the disease (Table 3). The best prognosis exists for lip cancer, with a 97% five-year relative survival rate if the tumor is localized and completely excised. Patients with oropharyngeal cancers with distant metastases are estimated to have only a 26.5% relative survival rate.

![Figure 1. Leukoplakia](image)

**Initial lesions: signs and symptoms**

Preventing disease progression relies on early detection, a diagnosis, and appropriate treatment. Early detection of oral cancer is complicated by the fact that many lesions in their earlier stages may be completely asymptomatic. For example, carcinoma of the maxillary sinus may remain undetected until an ulcer presents palatally. Symptoms of oral cancer, if they are present, can include pain, paresthesia, anesthesia, and difficulty in performing various oral functions, e.g., chewing (Table 5).

Clinically, cancerous and pre-cancerous lesions may present as ulcers, leukoplakia, erythroplakia, erythroleukoplakia, soft tissue masses, or other lesions that will not heal even after removal of the presumptive etiology, such as a defective restoration or ill-fitting denture (Figures 1–3). Any abnormal unexplained radiolucency is suspect until proven otherwise.

![Figure 5a. Signs of oral cancer](image)

Table 3. Five-year survival rate by stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Five-year survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>81.80%</td>
</tr>
<tr>
<td>Regional</td>
<td>52.10%</td>
</tr>
<tr>
<td>Distant</td>
<td>26.50%</td>
</tr>
<tr>
<td>Unstaged</td>
<td>46.2%</td>
</tr>
<tr>
<td>Overall</td>
<td>59.10%</td>
</tr>
</tbody>
</table>


Survival rates also depend on the cancer’s site (Table 4). Lip cancer usually presents as a lesion that fails to heal and is obvious to the patient and clinician alike, and has a high survival rate if diagnosed early and treated appropriately. Oral cancers in other anatomic sites can be clinically occult and asymptomatic. Fifty percent of tongue carcinomas have metastasized by the time they are diagnosed, and within five years a further 20% metastasize.17

It is clear that early diagnosis of oral cancers significantly improves the patient’s long-term survival. Early diagnosis also reduces morbidity and can minimize the extent of treatment required. While in other anatomic sites in the body malignancies can be radically excised, the excision of an oral cancer, depending on the site and size of the tumor, can severely compromise the patient’s quality of life and in some cases may not even be possible.

![Figure 5b. Symptoms of oral cancer](image)

Table 4. Five-year relative survival rate by site and stage of disease

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Local-</th>
<th>Regional</th>
<th>Distant</th>
<th>Unstaged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tongue</td>
<td>54.30%</td>
<td>73.60%</td>
<td>46.80%</td>
<td>25.90%</td>
<td>42.30%</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>59.70%</td>
<td>80.90%</td>
<td>47.70%</td>
<td>27.20%</td>
<td>54.10%</td>
</tr>
<tr>
<td>Salivary gland</td>
<td>51%</td>
<td>65.30%</td>
<td>53.30%</td>
<td>28%</td>
<td>38.50%</td>
</tr>
<tr>
<td>Lip</td>
<td>93.80%</td>
<td>97%</td>
<td>80.20%</td>
<td>35.30%</td>
<td>89%</td>
</tr>
<tr>
<td>Gum, other mouth</td>
<td>73.90%</td>
<td>94.20%</td>
<td>58.60%</td>
<td>32.70%</td>
<td>56.60%</td>
</tr>
<tr>
<td>Other oral cavity, pharynx</td>
<td>29.90%</td>
<td>49.20%</td>
<td>29.50%</td>
<td>4.70%</td>
<td>32.50%</td>
</tr>
<tr>
<td>Other oro-, nasopharyngeal</td>
<td>29.2%—52.8%</td>
<td>49.2%—78.5%</td>
<td>30.4%—57.6%</td>
<td>12.9%—30.6%</td>
<td>28.8%—51.7%</td>
</tr>
</tbody>
</table>

Adapted from: SEER Cancer Statistics Review 1975–2004

![Figure 5a. Signs of oral cancer](image)

<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukoplakia</td>
<td>None</td>
</tr>
<tr>
<td>Erythroplakia</td>
<td>Pain</td>
</tr>
<tr>
<td>Erythroleukoplakia</td>
<td>Paresthesia</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Numbness</td>
</tr>
<tr>
<td>Soft tissue mass</td>
<td>Difficulty in chewing</td>
</tr>
<tr>
<td>Unexplained radiolucency</td>
<td>Difficulty in eating</td>
</tr>
<tr>
<td></td>
<td>Difficulty in speaking</td>
</tr>
</tbody>
</table>

Table 5. Signs of oral cancer and symptoms
Leukoplakia, erythroplakia, and erythroleukoplakia (speckled leukoplakia) are clinical terms for white, red, or mixed red/white lesions, respectively, that cannot be wiped off, do not have an obvious clinical diagnosis, and have an unclear etiology. Leukoplakia is found in approximately 3% of adults. An estimated 85% of oral premalignant and malignant lesions present clinically as leukoplakias. The rate of malignant transformation of leukoplakia is estimated to be 7%, occurring on average seven years following initial diagnosis. The American Cancer Society estimates that up to 25% of leukoplakias are premalignant or malignant. Up to 42% of leukoplakias that contain dysplasia will eventually undergo malignant degeneration. Holmstrup et al. followed patients with oral premalignant lesions for up to 18.6 years (mean of 6.8 years) and found that non-homogenous leukoplakia had a seven times greater risk of malignant degeneration than homogenous leukoplakia. Lesions greater than 2 cm in size had a 5.4 times greater risk of developing malignancy than smaller lesions. In the case of erythroplakias, 70% to 90% have been found to be severely dysplastic or frankly malignant at the time of initial biopsy. The definitive diagnosis of oral cancer can only be determined by histopathologic examination of a biopsy specimen. The microscopic diagnoses range from normal, through varying degrees of dysplasia (mild, moderate, or severe), to carcinoma-in-situ to invasive malignancy. Oral cancers are given histopathologic grades which correlate with differentiation of the tissue and the clinical aggressiveness of the lesion (Figures 4, 5).

The detection of suspicious lesions is increased through routine, regular screening of patients. Early detection of suspicious lesions will result in earlier diagnosis, less aggressive treatment, and decreased need for complicated post-treatment management. The primary goal is to diagnose lesions. The secondary goal is to diagnose the malignancy before it metastasizes. The tertiary goal, emanating from the first two, is to minimize the morbidity associated with treatment and management in order to maximize the patient’s quality of life and survival.

**Early detection and technology**

Historically, unaided visual examination, palpation, and radiographs were available for oral cancer screening. In recent years, screening technologies have become available that supplement the visual examination and help the clinician identify suspicious lesions that require further investigation. In addition, non-invasive technologies are being investigated, including the use of saliva tests and dielectrophoresis to detect oral squamous cell carcinoma. Other technologies include the use of special wavelength lights and chemiluminescence, as well as dyes that selectively stain lesions. Stand-alone screening devices include the Microlux/DL (AdDent), VELScope (LED Dental, Inc.), and ViziLite and ViziLite Plus (Zila Pharmaceuticals, Inc.).

**Microlux/DL**

Microlux/DL is a hand-held device that uses light-emitting diodes (LEDs) as the illumination source. Prior to
exposing the mucosa to the light, the patient rinses for 30–60 seconds with 1% acetic acid. Upon illumination, the abnormal tissue will appear white (“aceto-white”).

VELScope
VELScope is a hand-held device that emits a blue light to fluoresce the mucosa. No pre-rinse is required. The amount of fluorescence depends on the health of the mucosa. When exposed to the blue light, normal mucosa emits a pale green autofluorescence, while abnormal tissue appears dark green to black (Figures 6a, b). Highly inflamed mucosa results in a loss of fluorescence which may result in a false positive.30 Using this device can facilitate detection of a lesion that otherwise may have been missed. The VELScope has been found to help delineate the extent of visible lesions, as well as to identify lesions that were difficult to appreciate with unaided visual examination.31 In one study, 12 of 19 VELScope-positive lesions were biopsied and found to exhibit loss of heterozygocity.32

ViziLite and ViziLite-Plus
ViziLite is a hand-held device that emits chemiluminescent light. The patient rinses for 30–60 seconds with 1% acetic acid and the ViziLite device is used to illuminate the oral cavity. Abnormal areas will appear white (“aceto-white”). The light increases both the brightness and the sharpness of lesions (Figure 7).33

Figure 6a. Lesion prior to use of VELScope  Figure 6b. Appearance following autofluorescence

Figure 7. “Aceto-white” appearance with use of ViziLite

Chemiluminescence has been found to significantly assist the clinician in identifying white and erythropleukoplastic lesions. In one study of 134 patients, use of ViziLite identified two lesions that were not found by unaided visual examination, one of which was a squamous cell carcinoma of the tongue.34 Kerr et al. studied 501 patients and visually found 410 lesions in 270 patients, with 31% being deemed suspicious and meriting further evaluation. Ninety-eight lesions were found when ViziLite was used with 77 of these considered suspicious, including six that had been missed with unaided visual examination.35 The adjunctive use of T-Blue630 is a feature specific to the ViziLite-Plus system. This is the only FDA-cleared device and in-vivo staining system for the marking and identification of oral lesions. T-Blue630 is the brand name for pharmaceutical-grade toluidine chloride, a toluidine blue dye. After using the ViziLite to identify abnormal “aceto-white” areas, T-Blue630 can be used to mark suspicious areas for further evaluation, e.g. biopsy (Figures 8a, b; Figures 9a, b).36 While generic toluidine blue is available, it is not FDA-cleared for human use. Other stains such as methylene blue are also not FDA-cleared for this use.

Toluidine blue
Toluidine blue is a vital tissue dye which exhibits differential uptake into tissue, resulting in metabolically active areas of lesions being stained a deep blue. Adjunctive use of T-Blue630 helps identify abnormal lesions, facilitates biopsy site selection and eventual definitive diagnosis.

Toluidine blue has been found to be particularly effective at differentially staining the nuclei of premalignant and malignant oral epithelial neoplasms (squamous cell carcinomas).37 No observed staining pattern is seen for stained benign lesions.38 Epstein et al. found that use of toluidine chloride (toluidine blue) was more sensitive than visual examination in identifying lesions in patients with prior upper aerodigestive tract malignancies.39 Patients find the use of toluidine blue an acceptable procedure. One
survey found 95% of patients wished to continue with these screenings in the future.40

Toluidine blue is effective at delineating malignant tumor borders, thereby aiding the identification of abnormal cells present beyond the lesion’s visible border. Missmann et al. identified abnormal and premalignant cells more than 1 cm from the lesion using toluidine blue, allowing for a larger resection to remove these cells that would otherwise not have been detected by visual examination alone.41 Another study that involved 50 patients used toluidine blue to stain surgical margins following resection of malignant tumors and found malignant cells still remaining following presumptive excision. In occasional cases toluidine blue also stained traumatized mucosa resulting in a false positive result.42 Onofre et al. found toluidine blue to be highly predictive, with no false negatives for either SCCA or carcinoma-in-situ.43 Epstein et al. found that the use of toluidine blue resulted in no false negatives and that 100% of lesions that were histopathologically determined to be carcinoma-in-situ or invasive malignancies stained positively. In contrast, unaided visual clinical examination detected only 78% of these lesions.44 It is significant for clinicians to realize that if a lesion does not stain with toluidine blue, but remains clinically suspicious for two weeks, it should still be biopsied as false negatives can occur. Toluidine blue may also aid monitoring of patients for recurrent oral cancer but is of limited use in areas with postoperative scarring where a reconstructive flap has been placed.45

**Screening protocol**

Early detection of oral cancer and related premalignancy requires an appropriate screening and diagnosis protocol. It has been recommended that all adult patients 18 and over be screened annually,46 even if medical and dental histories elicit no risk factors. Known-risk patients should be screened every six months. The strong association between HPV and oral cancer further underscores the need to screen all patients, as there is a likelihood that risk of HPV transmission will not be elicited by a medical history taken in the dental office setting. The screening protocol should include medical and dental history, unaided and aided visual examination, and palpation (Figure 10). All oral structures must be thoroughly examined, and any abnormalities should be recorded on a mouth map. If suspicious lesions are found during the screening procedure, the lesion must be biopsied or the patient referred to a specialist for further evaluation.

**Biopsy protocol**

The two basic biopsy techniques for definitive diagnosis of oral mucosal lesions are incisional biopsy and excisional
biopsy. The brush biopsy (CDx) is a third type of biopsy that can be used as a preliminary diagnostic tool. The brush biopsy uses a stiff brush to obtain a full-thickness sampling of epithelial cells for examination, in patients with mucosal lesions. The brush biopsy may also be useful as an intermittent preliminary diagnostic technique in patients under observation. While brush biopsies are practical, simple to perform, and less invasive than an incisional or excisional biopsy, they are insufficient to provide a definitive diagnosis. Incisional or excisional biopsy is the standard-of-care for definitive diagnosis.

Mucosal lesions that are microscopically confirmed to be benign must still be evaluated regularly for progression. In this regard, the ability to predict risk of the lesion undergoing malignant transformation could help determine the frequency of follow-up and/or earlier intervention.

Risk differentiation and prediction

Dysplasia and risk prediction

The conventional wisdom is that the more severe a lesion’s dysplasia, the more likely it is that it will undergo malignant transformation. (Conversely, the less severe the dysplasia, the less likely that the lesion will undergo malignant transformation.) A number of recent studies do not support this presumption. Holmstrup et al. did not find any degree of dysplasia, or site and delineation of the lesion, as a statistically significant predictor of malignancy. Scully et al. have stated that while dysplasia can be predictive, that this is not always the case. They also pointed out that variability in determining the diagnosis exists between examiners as well as by the same examiner. Rosin et al. studied biopsies and outcomes for patients with secondary premalignant lesions following treatment for primary oral cancer and found that the initial microscopic classification of the leukoplakia at the previously treated site did not predict a secondary oral malignancy. Forty-seven percent of leukoplakias classified as having either no dysplasia or mild dysplasia developed into a secondary oral malignancy. Primary tumor stage, grade, and location were not significantly associated with the outcome.

In patients with a previous history of oral cancer, recurrences can occur at the initial site or further away and may or may not be related. Adjacent mucosa that appears clinically normal has been found to harbor genetically-altered cells with loss of heterozygocity. While a number of cancers recur due to incomplete excision of the actual lesion, it has also been suggested that premalignant cells are able to migrate to a different site outwith the original lesion’s area.

Chromosomal abnormalities and risk prediction

Lesions that undergo malignant transformation lose cell cycle regulation and genetic changes are evident. Recent microscopic studies have investigated loss of heterozygocity (LOH) in tumor cells and its potential role as a risk predictor for malignant transformation. A number of chromosomal abnormalities are now known to be predictive of high risk of oral cancer. LOH has been found to indicate high risk of transformation or conversion to malignancy. In particular, aberrations in the 3p, 9p, and 17p chromosomal arm sites have been implicated as high-risk predictors, although other chromosomal arm alterations also occur. Rosin et al. examined biopsies and outcomes for patients with secondary premalignant lesions. They found that LOH in multiple chromosome arms, and in particular in 3p and 9p sites, was predictive of a secondary malignancy. Aberrations in multiple arms rather than in single arms are believed to increase that risk.

Risk prediction and treatment planning

Given that specific chromosomal and genetic alterations have been found to be predictive of the risk of malignancy developing in a premalignant lesion, histopathologic assessment of these changes will help to identify those patients most at risk in the future and enable tailored case management.

Several investigators have found correlations between the degree of toluidine blue dye uptake and the presence of chromosomal alterations. Zhang et al. monitored premalignant lesions, for on average 44 months, in 100 patients with no prior oral cancer history. Toluidine blue staining was associated with a 600% increased risk of transformation and occurred in 80% of the lesions that later became malignant. The association of stain and risk factors also applied to lesions initially showing no or mild dysplasia. Epstein et al. studied 32 patients with oral lesions who were biopsied following dye retention. They studied lesions with LOH on three chromosome arms (3p, 9p, and 17p). Toluidine blue positive-stained lesions demonstrated LOH more frequently than dye-negative lesions in 3p and 9p, and more dye-positive cases had LOH on multiple chromosome arms, associated with an increased risk of malignancy (Figures 11a, b). Based on these studies, differential uptake of toluidine blue is associated with chromosomal changes and LOH rather than simply malignancy and/or the degree of dysplasia, and may be a useful adjunct in the future for risk prediction.

Summary

The importance of routine screening to improve early diagnosis of oral malignancies cannot be overemphasized. It is incumbent upon the clinician to screen all adult patients for oral cancer. Available screening technologies cleared for human use by the FDA include the use of LED lights, autofluorescence, chemiluminescence, and the combined
use of chemiluminescence and T-Blue. Toluidine blue aids in the visual identification of suspicious lesions. Recent advances have shown that the risk of malignant transformation is associated with chromosomal aberrations. Lesions staining positive for toluidine blue exhibit these genetic changes. The ability to identify lesions and to predict which lesions will undergo malignant transformation would facilitate early diagnosis and subsequent disease management tailored to the individual patient. The ultimate goals are to reduce both mortality and morbidity, and to improve patients’ quality of life.

References
21 Silverman S. Oral Cancer. 5th ed.


**Author Profile**

**Denis P. Lynch, D.D.S., Ph.D.**

Dr. Lynch received his Doctor of Dental Surgery degree from the University of California at San Francisco in 1976. He subsequently completed a residency in oral and maxillofacial pathology at the University of Alabama at Birmingham, as well as a Ph.D. in Experimental Pathology.

Dr. Lynch joined the faculty of the University of Texas Dental Branch at Houston in 1981, eventually serving as Executive Associate Dean. In 1993 he went to the University of Tennessee Memphis as Executive Associate Dean of the College of Dentistry and served as both Professor of Dentistry and Professor of Medicine until 2002. Dr. Lynch is currently Professor of Oral and Maxillofacial Pathology and Associate Dean for Academic Affairs at Marquette University School of Dentistry in Milwaukee, as well as Professor of Dermatology at the Medical College of Wisconsin. He is the author of numerous scientific articles and book chapters, as well as the coauthor of *The Mouth: Diagnosis and Treatment*.

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**Acknowledgement**

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1. In the United States, more than _____ new cases of oropharyngeal cancer will be diagnosed in 2007.
   a. 17,000
   b. 26,000
   c. 34,000
   d. 42,000

2. The most common site for oral cancer in patients in the United States is
   a. the tongue
   b. the cheek
   c. the lip
   d. a and c

3. The single greatest risk factor for oral cancer in the United States is
   a. drinking
   b. use of tobacco
   c. use of narcotics
   d. a and c

4. A reduced risk of oral cancer has been associated with a high dietary fruit and vegetable intake.
   a. True
   b. False

5. A viral risk factor associated with oral cancer is the _____.
   a. hepatitis virus
   b. human papillomavirus (HPV)
   c. human immunodeficiency virus (HIV)
   d. b and c

6. The overall five-year relative survival rate for oropharyngeal cancer diagnosed between 1996 and 2003 is estimated to be _____.
   a. 51.1%
   b. 59.1%
   c. 62.3%
   d. none of the above

7. The five-year relative survival rate for oral cancer is higher than the five-year relative survival rate for breast cancer.
   a. True
   b. False

8. Early diagnosis of oral cancer _____.
   a. reduces morbidity
   b. reduces mortality
   c. can minimize the extent of treatment required
   d. all of the above

9. Clinical signs of oral cancer may include _____.
   a. leukoplakia
   b. green mucosa
   c. difficulty in speaking
   d. a and c

10. Clinical symptoms of oral cancer can be _____.
    a. no symptoms
    b. numbness
    c. difficulty in eating
    d. all of the above

11. Leukoplakia is estimated to _____.
    a. be found in approximately 3% of adults
    b. be the clinical presentation in 85% of oral premalignant and malignant lesions
    c. have a 7% rate of malignant transformation
    d. all of the above

12. Non-homogenous leukoplakia has a greater risk of malignant degeneration than homogenous leukoplakia.
    a. True
    b. False

13. The definitive diagnosis of oral cancer can be determined by _____.
    a. brush biopsy
    b. incisional or excisional biopsy
    c. visual and clinical examination
    d. all of the above

14. The detection of suspicious lesions is increased through regular screening.
    a. True
    b. False

15. The primary goal of screening for oral cancer is _____.
    a. diagnosis
    b. treatment
    c. the protocol
    d. all of the above

16. _____ is being investigated as a non-invasive oral cancer screening technology.
    a. Saliva testing
    b. Periodontal disease
    c. Dielectrophoresis
    d. a and c

17. Stand-alone oral cancer screening devices currently available include _____.
    a. ViziLite Plus
    b. VELScope
    c. Ultrascope
    d. a and b

18. _____ is cleared by the FDA as a stain for the marking of oral lesions.
    a. Tolu dine blue
    b. Methylene blue
    c. T-Blue630
    d. all of the above

19. Several studies have shown that use of ViziLite aids identification of lesions not found with unaided visual examination.
    a. True
    b. False

20. Adjunctive use of T-Blue630 can _____.
    a. help identify abnormal lesions
    b. facilitate biopsy site selection
    c. provide a definitive diagnosis
    d. a and b

21. Toluidine blue is effective in _____.
    a. delineating malignant tumor borders
    b. differentially staining the nuclei of premalignant oral epithelial lesions
    c. staining subgingival calculus
    d. a and b

22. If a lesion does not stain with toluidine blue and remains clinically suspicious after two weeks, _____.
    a. it should still be biopsied
    b. it does not need to be biopsied
    c. it should be biopsied if it is still present in six months
    d. none of the above

23. Known-risk patients should be screened more often than patients with no known risk.
    a. True
    b. False

24. A screening protocol should include _____.
    a. a medical and dental history
    b. visual examination
    c. palpation
    d. all of the above

25. Holmstrup et al. did not find any degree of dysplasia a statistically significant predictor of malignancy.
    a. True
    b. False

26. Rosin et al. found that _____ of leukoplakias in previously treated sites with either no dysplasia or mild dysplasia developed into a secondary oral malignancy.
    a. 25%
    b. 38%
    c. 47%
    d. 53%

27. Lesions that undergo malignant transformation _____.
    a. lose cell cycle regulation
    b. evince genetic changes
    c. are rare
    d. a and b

28. Aberrations on certain chromosomal arms have been found to be high-risk predictors of malignant transformation.
    a. the degree of toluidine blue dye uptake
    b. geographic origin
    c. sex of the patient
    d. b and c

29. A number of investigators have found a correlation between _____ and the presence of chromosomal alterations.
    a. the degree of toluidine blue dye uptake
    b. geographic origin
    c. sex of the patient
    d. b and c

30. The ability to predict lesions at high risk of malignant transformation would _____.
    a. facilitate disease management
    b. be relatively unimportant
    c. facilitate early diagnosis
    d. a and c
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**Educational Objectives**

1. Know the incidence of oral cancer in the United States and understand the risk factors.
2. Be knowledgeable about signs and symptoms of oral cancer.
3. Understand screening methods available for the detection of oral cancer.
4. Understand the role of chromosomal aberrations in the risk of malignant transformation.

**Course Evaluation**

Please evaluate this course by responding to the following statements, using a scale of Excellent = 5 to Poor = 0.

1. Were the individual course objectives met?  
   - Objective #1: Yes No  
   - Objective #2: Yes No  
   - Objective #3: Yes No  
   - Objective #4: Yes No

2. To what extent were the course objectives accomplished overall?  
   - 5 4 3 2 1 0

3. Please rate your personal mastery of the course objectives.  
   - 5 4 3 2 1 0

4. How would you rate the objectives and educational methods?  
   - 5 4 3 2 1 0

5. How do you rate the author’s grasp of the topic?  
   - 5 4 3 2 1 0

6. Please rate the instructor’s effectiveness.  
   - 5 4 3 2 1 0

7. Was the overall administration of the course effective?  
   - 5 4 3 2 1 0

8. Do you feel that the references were adequate?  
   - Yes No

9. Would you participate in a similar program on a different topic?  
   - Yes No

10. If any of the continuing education questions were unclear or ambiguous, please list them.

11. Was there any subject matter you found confusing? Please describe.

12. What additional continuing dental education topics would you like to see?

**PLEASE PHOTOCOPY ANSWER SHEET FOR ADDITIONAL PARTICIPANTS.**

**Mail completed answer sheet to**

Academy of Dental Therapeutics and Stomatology,  
A Division of PennWell Corp.  
P.O. Box 116, Chesterland, OH 44026  
or fax to: (440) 845-3447

For IMMEDIATE results, go to www.ineedce.com and click on the button “Take Tests Online.” Answer sheets can be faxed with credit card payment to (440) 845-3447, (216) 398-7922, or (216) 255-6619.

- Payment of $59.00 is enclosed.  
  (Checks and credit cards are accepted.)

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CANCELLATION/REFUND POLICY

Any participant who is not 100% satisfied with this course may request a full refund by contacting PennWell in writing.  

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