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Oral Cancer Diagnostic Technologies

Learning Objectives

A. Discuss the value of early oral cancer diagnosis

B. Describe the chairside technology available to help identify possible pre-cancerous/cancerous lesions

C. Compare and contrast the technologies and the evidence supporting their use

Introduction

Oral cancer statistics are stark. The Oral Cancer Foundation estimates 35,000 cases of oral or pharyngeal cancer this year in the U.S. alone, and estimates approximately 8000 deaths.[1] 50% of those newly identified with oral cancer will not live past five years after initial diagnosis. These statistics equate to one North American dying from oral cancer every hour of every day, and the prognosis has shown little improvement over the last thirty years. While we often hear about cervical, testicular, and skin cancer in the media and from health care providers, the chance of dying from oral cancer is actually greater than any of these other diseases. As of 2004, oral cancer is the 6th leading cause of cancer deaths.[2]

The number of malpractice claims "alleging failure to diagnose oral cancer" is rising. These claims rank among the most expensive for the dentist. These cases can prove difficult to defend, in part because juries tend to believe the argument that dental professionals can easily and inexpensively perform oral cancer screenings on a regular basis.[3]

When diagnosed early the oral cancer survival rate can be 80% to 90%, but currently only 35% of cases are caught in time to improve prognosis. Diagnosing oral cancers earlier, even at stage II, not only would improve the lives of patients, but also help ease the financial and emotional healthcare bind facing the country.[4]

Oral cancers include intraoral melanomas and Kaposi's sarcoma, but most are squamous cell carcinomas. Early identification of oral cancers and precancers proves difficult because clinical characteristics of early lesions are subtle. Premalignant lesions often present as familiar benign conditions, and many are not discernable by the eyes alone.[5]

Certain chairside diagnostic technologies and tests have entered the commercial market over the last ten years. Others are still being developed. This course aims to describe the different adjunct techniques and tests available to the dental professional in order to help identify cancerous and precancerous lesions earlier.

Patient Profile

The patient populations with the highest risk for oral cancer include people who:

- have a history of oral cancer
- are 40 and over (although oral cancer is increasing in the 18-49 demographic)
- use tobacco and alcohol
- have premalignant lesions or dysplasia

In the past, men were 6 times more likely to have oral cancer than women, but the ratio of male to females with the disease is now 2:1. African Americans, non-Hispanic Caucasians, Vietnamese, and Native Hawaiians experience oral cancer most frequently. Incidence rates based on socio-economic factors do not currently exist. It appears that lifestyle factors have the biggest impact on the development of oral cancer.[6] A study published in 2008 analyzed data from the California Cancer Registry in order to determine incidence rates of oral squamous cell carcinomas (OSCCs). The research is the first to examine OSCC rates of cultural subpopulations within the state. Black Non-Hispanics and White Non-Hispanics have the highest incidence rates of cancer of the tongue and the floor of the mouth. Of Asian subpopulations, South Asians were most likely to have cancer of the tongue, with male and female incidence rates being quite similar in number. Interestingly, Filipino women acquired palatal cancer more than any other group. While the study was not designed to discover the etiology of the cancer, the researchers suggest that cultural habits, particularly with regard to tobacco and alcohol use, could possibly coincide with the relative incidence rates of OSCC.[7]

Risk Factors and Cofactors

Tobacco, smoked and smokeless, is implicated in 90% of oral cancer cases involving a risk factor. Its use increases the risk for developing squamous cell cancer 8 to 20 fold.[8] According to a study from University of California, San Francisco, nearly nine out of ten patients with oral cancer have previously smoked.[9]

Despite marketing claims that smokeless tobacco is a safer alternative to smoking with regard to lung cancer, smokeless tobacco has a negative effect on the incidence rates of oral cancers and periodontal disease. The U.S. Department of Health and Human Services has included smokeless tobacco on the list of known carcinogens.[10] In addition, research suggests that smokeless tobacco produces chronic infections that might also be linked to heart disease and high blood pressure.[11] While smokeless tobacco is a habit often attributed to men, women

also use it. In 2001, the National Institute of Drug Abuse reported that nearly 600,000 adolescent and adult females use the substance.[12]

Alcohol use is implicated as a synergistic cofactor with tobacco. Alcohol alone increases the risk of oral cancers 6 times, according to the Centers for Disease Control. When used with tobacco, however, the risk of squamous cell carcinomas increases dramatically.[13]

In addition to tobacco and alcohol use, Human Papillomavirus strain 16 (HPV16) has been reported in 18.9% of oropharyngeal cancers and 3.9% of oral cavity cancers.[14] The Johns Hopkins Oncology Center reported results from a study testing tissue from 253 head and neck cancer patients for strains of HPV. The Human Papillomavirus was found in 25% of patients, and of that subset, 90% of the tissues tested positive for HPV16.[15] This association is significant because the number of Americans infected with HPV has reached 20 million. The CDC expects an additional 6.2 million to acquire HPV each year.[16]

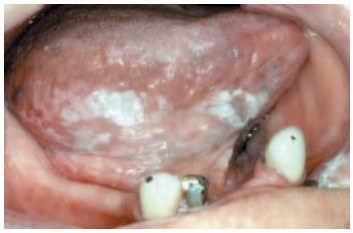
The Oral Cancer Foundation notes that a history of oral cancer is a risk factor in and of itself. First-time cancer survivors face a heightened risk of a second cancer that may continue for five to ten years from the first incident.[17]

Signs and Symptoms

Common symptoms of oral cancer include:

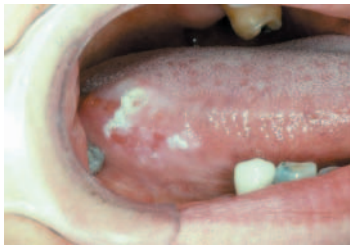
- Patches inside the mouth or on the lips that are white (leukoplakia), a mixture of red and white (erythroleukoplakia), or red (erythroplakia)
- A sore on the lip or in the mouth that will not heal
- Bleeding in the mouth
- Loose teeth
- Difficulty or pain when swallowing
- Difficulty wearing dentures
- A lump in the neck
- An earache
- Advanced lesion characteristics

Other signs include a range of characteristics including a painless ulcer, papillary growth, indurated section with little to no surface alterations, tongue fixation, restriction on opening the mouth due to decreased tissue mobility, tooth and lower lip paresthesia (if nerve involvement).[18]



Leukoplakia on lateral border of the tongue

Leukoplakias are the most common oral premalignant lesions, and sometimes become malignant. The rate of malignant transformation is approximately 7%, and the mean time for malignant transformation is seven years. The rate of malignant transformation for leukoplakia with dysplasia is almost 37%.[19] The American Cancer Society reports that roughly 25% of leukoplakias are pre-cancerous or cancerous.[20]

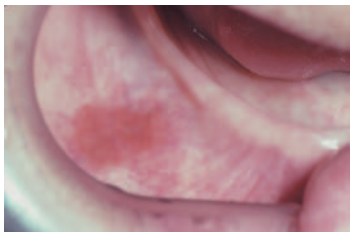


Erythroleukoplakia on lateral border of the tongue

The progression to malignancy increases with erythroleukoplakias and erythroplakias, respectively. Ninety-one percent of erythroplakias have severe dysplasia or worse.[18] The American Cancer Society states that "as many as 7 out of 10 [erythroplakias] turn out to be cancer when they are biopsied or will develop into cancer later."[21]

Precancerous or premalignate conditions fall into two categories: dysplasia and carcinoma-in-situ (CIS). Dysplasia is defined as an abnormality of development in pathology, alteration in size, shape and organization of adult cells above the basement membrane. The condition is categorized as mild, moderate, or severe. Mild dysplasia involves the basal 1/3 of the epithelium. Moderate involves the basal 2/3. When 95% of the epithelium is involved, then the dysplasia is deemed severe.

A carcinoma-in-situ lesion involves the full thickness of the epithelium, but cancerous cells have not broken through the basal membrane. When the cancer or cells invade past the basal membrane, the lesion is either a carcinoma or sarcoma. Most are oral squamous cell carcinomas.



Courtesy of Dr. Lane Thomsen

Carcinoma-in-situ in an edentulous patient

Cancer Stages

If a premalignant lesion evolves into a carcinoma, researchers and health professionals use a categorized staging system to describe how severe a cancer is, and whether it has spread or remained localized. Different staging systems exist, but this article and the literature cited within it use the following system to describe oral cavity and lip cancers:[22]

- Stage I – The cancer does not span more than 2 cm, and has not metastasized (spread) to local lymph nodes
- Stage II – The cancer spans between 2 and 4 cm, and has not metastasized to local lymph nodes
- Stage III – The cancer spans more than 4 cm, or the cancer is any size but has metastasized to a single, lymph node in the neck region ipsilateral (on the same side) to the original cancer. The cancerous lymph node does not exceed 3 cm.

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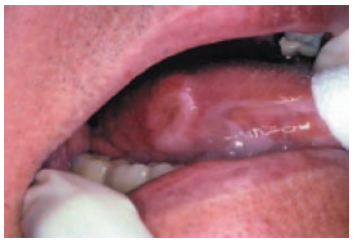
- Stage IV – Any of the following applies: a) The cancer has spread within the oral cavity or to the lips; the local lymph nodes may or may not be involved. b) The cancer measures any size, and has spread: to multiple, local lymph nodes ipsilaterally, to local lymph nodes on one or both sides of the neck, or to any lymph node exceeding 6 cm.) The cancer has metastasized to other body regions.



Oral Squamous Cell Carcinoma (OSCC)

- Recurrent – The cancer returned after treatment, to the same or different part of the body

Areas of greatest risk

Oral cancers can occur on any mucosal site. Typically, they occur in a U-shaped zone from the tonsillar pillars and lateral soft palate, to the lateral tongue, and ending at the anterior floor of the mouth.

The relative incidence rates of oral squamous cell carcinomas are as follows: [23]

- Tongue - 25%
- Lower Lip (vermilion) - 30-40%
- Floor of mouth - 20%
- Oropharynx/soft palate - 15%

Tobacco and alcohol-related lesions are often located in different areas of the oral cavity compared to HPV-related lesions. Tobacco and alcohol-related lesions are usually found on the anterior tongue, floor of the mouth, buccal mucosa, and alveolar ridges. HPV-related oral squamous cell carcinomas, on the other hand, appear towards the posterior regions of the oral cavity (base of the tongue, oropharynx, tonsils, and tonsillar pillars).[24]

Conventional Oral Cancer Examinations and Diagnostic Technologies

For conventional oral examinations, a health practitioner visually examines the oral cavity with incandescent light, gauze, a mouth mirror, and magnification. Nearly all dental practitioners report that they regularly exam their patients for oral cancer, and yet only 15% of patients reported receiving an oral cancer examination on an American Dental Association survey. Horowitz & Califano (2001) report approximately 20% of the American population are examined for oral cancer as a part of basic treatment procedures, with Black, Hispanic and patients with less formal education less likely to be checked. The true percentage of practitioners who regularly perform these examinations is probably higher. Some patients may not understand that the common Extra Oral/Intra Oral exam is intended to screen for oral cancer, but rather assume it is a simple check for decay or other dental issues. These authors also report some health care professionals choose not to screen patients, perceiving the exam as time consuming, or fearing that performing the exam could leave them liable for inaccuracy.[25]

Regardless, early detection is the key to decreasing both morbidity and mortality associated with Stage I and II squamous cell carcinomas and oral premalignant lesions. Pre-cancerous epithelial lesions can remain undetected clinically for years until they progress to the surface. If detected before they reach the surface, however, the treatment for these early lesions is generally less aggressive, and leaves the patient with a better quality of life post-treatment.

A debate continues over whether the conventional oral examination is truly useful for early detection of oral cancers. One randomized, controlled study showed a significant rate of survival when patients with risky lifestyle choices, such as tobacco use, were screened. However, issues arise especially with leukoplakias and erythroplakias. Finding the hidden lesions, or distinguishing between the benign versus premalignant atypical lesions which appear in 5-15% of patients, proves difficult.[26] There is no way to distinguish which lesions have the ability to transform into malignancies with a conventional oral examination alone.

Certain detection technologies can be used as adjuncts in order to help identify those lesions that might progress into cancer. The equipment is not intended for definitive diagnosis, and cannot be substituted in lieu of a scalpel biopsy, the gold standard. However, the adjuncts can help identify abnormalities in a non-invasive manner with a reasonable level of accuracy.[27]

Diagnostic Aids and Tests

The chairside adjuncts and tests available include light-based detection systems, fluorescence visualization, and brush cytology. Advancements in saliva testing are also showing positive initial results. Ideally, an adjunct or test has high sensitivity and specificity, meaning few false positives and false negatives, respectively. The proportion of subjects with positive test results for the disease determines sensitivity. The proportion of subjects clear of the disease, and also test negative, determines specificity.[28]

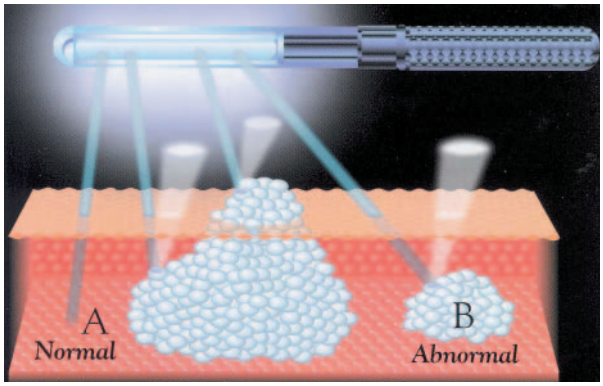
Light-based Detection Systems

Light-based detection systems use several chemiluminescence, blue-white LED, and autofluorescence as light sources. They are designed to detect possible abnormalities in the epithelial tissue that are not necessarily visible to the naked eye.

Chemiluminescent Light and Blue-White LED Systems

Three products, ViziLite® Plus (Zila Pharmaceuticals), Orascoptic DK™ (Sybron Dental), and Microlux/DL™ (AdDent Incorporated), use light-based detection. ViziLite® Plus uses a chemiluminescent light stick. Orascoptic DK™ and Microlux/DL™ use a blue-white LED fiber optic light. Each of these systems employs a 1% acetic acid rinse to dislodge foreign matter, and to make cell nuclei in the epithelium more prominent.

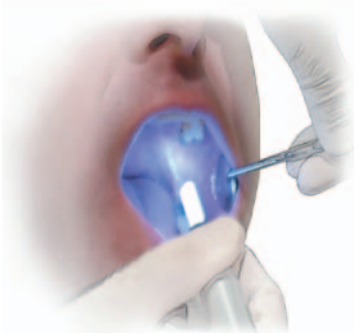
The patient rinses with the acid for 30-60 seconds. Then, with dimmed lights, a dental professional visually examines the oral cavity with the light source. Abnormal epithelium will appear exceedingly white (acetowhite). Under the light, normal epithelial tissue reflects a light bluish color. The test itself takes approximately five minutes, and can be performed by licensed dentists, hygienists, physicians, and nurses. The light can actively illuminate for ten minutes.



Chemiluminescence reflecting normal and abnormal tissue

ViziLite® Plus also includes TBlue630, a pharmaceutical grade tolonium blue dye that stains the potentially abnormal area for easier documentation and marking of the lesion after the blue-white light is gone. Tolonium chloride dye itself has also been used as an adjunct for identifying atypical tissue during oral exams. To date, TBlue630 has FDA approval for marking only, and is not intended to be used as a standalone adjunct product. ViziLite® Plus received FDA clearance as an adjunct aid for visual oral tissue examinations in populations with a higher oral cancer risk in 2001. Microlux/DL™ and Orascoptic DK™ do not include a dye for lesion marking.

With these systems, the appearance, location, history, and morphology of the lesion should be documented, and photographed, if possible. The lesion can then be watched for changes for two weeks, or referred directly for biopsy if something more severe is suspected.



Mouth lit by blue-white LED light stick

ViziLite® Plus Components

ViziLite® is sold in single-use kits including a disposable light stick and retractor, acetic acid solution, and TBlue630 marking system. The Microlux/DLTM kit includes a reusable, battery operated light source, a light guide, and six bottles of acetic acid. AdDent makes a disposable sleeve that fits over the entire Microlux/DLTM unit and light guide to reduce the risk of cross-contamination. The Orascoptic DK™ kit includes an LED light source, an oral lesion screening instrument, a transillumination instrument, lighted mirror, and six bottles acetic acid solution. The transillumination instrument and lighted mirror are autoclavable, but the light source is not. Custom plastic barrier sleeves are available. The transillumination instrument is primarily used to identify proximal caries.

TBlue630 kit components

ViziLite® Plus, Microlux/DLTM, and Orascoptic DK™ are contraindicated for those who might have difficulties understanding instructions, or who have physical impairments that might interfere with properly using the 1% acetic acid rinse or following instructions during the visual exam with the blue-white light guide. TBlue630 is contraindicated for the following groups:

- Lactating or pregnant women
- Those hypersensitive to TBlue630 ingredients
- Children
- People with renal or liver impairment

Licensed professionals (dentist, hygienist, physician, or nurse) can use ViziLite®, Microlux/DLTM, and Orascoptic DK™ because the tool is intended to be used as an adjunct. Further diagnosis, preferably from a scalpel biopsy, would be performed by the appropriate physician or surgeon.

Orascoptic DK™ kit

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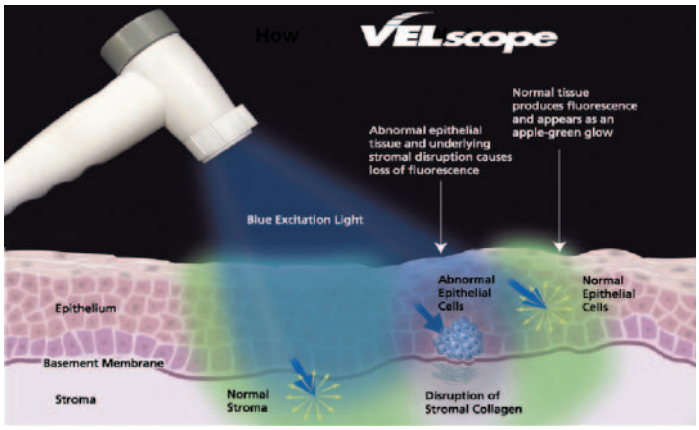
Numerous studies have tested the effectiveness of chemiluminescence and blue-white LEDs combined with the acetic acid rinse. In several, researchers report a fraction of lesions illuminated with the systems that were not detected in conventional oral exams with incandescent light.

Microlux/DL™ kit

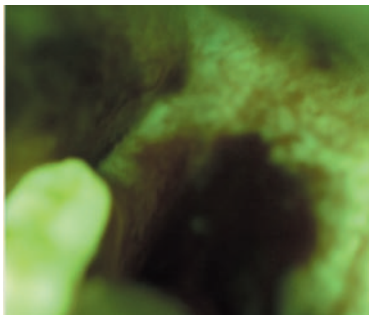
Fluorescence Visualization Technology

Another light-based detection technology is fluorescence visualization. Fluorescence, the mechanism of action of VELscope® (LED Dental, Inc), uses a specific wavelength of blue light, transmitted through a halide lamp, to excite tissue from the epithelial surface, down through the basement membrane, stopping at the stroma.



Fluorescence using VELscope® hand piece

The lighted tissue, in turn, emanates a green fluorescence (sometimes referred to as autofluorescence). The emitted fluorescence is not visible to the naked eye, but the VELscope® hand piece filters out the blue light, so that only the green fluorescence remains. Differences in the degree of green reveal possible abnormalities. Healthy tissue appears pale, lime green, while abnormal tissue appears dark green to dark rust.

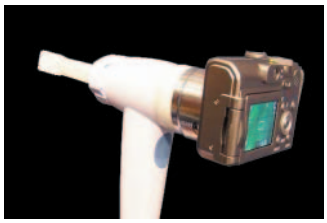


Rust colored lesions visible with VELscope®

Unlike the other light-based systems, the fluorescence does not require a pre-rinse. VELscope® does not come with the lesion-marking solution, such as TBlue630, but VELscope® allows for the adaptation of a digital camera to photograph lesions where they can then be stored or shared with various health practitioners. There are no contraindications for the use of fluorescence.

VELscope® is a portable unit that can be placed on a counter top or mobile cart to be transported to different operatories in an office or clinic. To prevent cross-contamination, VELscope® comes with inexpensive disposable caps and sheaths that protect the patient, practitioner, and unit. A disposable retractor helps access to the oral cavity, and includes markings for measurement of the lesion.

Direct fluorescence visualization has shown 98% sensitivity and 100% specificity, when verified by histology, in identifying "oral premalignant lesions and invasive squamous cell carcinomas."[29] While the lesions were also visible by regular, incandescent light, the fluorescence correctly identified suspicious Class I lesions.[30]

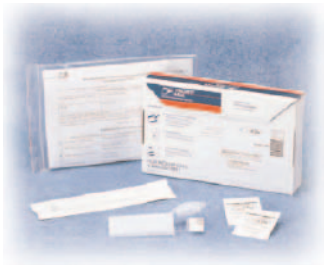


VELscope® with camera attached

The FDA approved VELscope® in 2006 as an adjunct to a conventional, incandescently lighted oral exam to aid detection of tissue abnormalities, such as cancer or OPLs, not necessarily visible without additional technology. VELscope® has also been approved for use by surgeons to help identify diseased margins of clinically visible lesions.

Brush Cytology

Brush cytology or transepithelial oral brush biopsy, is intended to detect asymptomatic, precancerous red and white dysplasias, chronic ulcers, and atrophic, thick, or traumatized mucosa (Class II lesions). According to the manufacturer, the test is not intended to be used for suspicious lesions, fibromas, mucoceles, hemangiomas, submucosal masses, or pigmented lesions (Class I lesions).[31]



Oral CDx® The Brush Kit

A sample of the lesion is collected with a small brush. The brush is placed against the lesion, and rotated 5-15 times with firm pressure. (The area biopsied will become pink, and might have some pinpoint bleeding.)[32] The collected tissue is placed on a dry slide, fixed, and sent in a provided envelope to the OralScan Laboratories in Suffern, NY, to be evaluated by a trained pathologist after computer analysis. An atypical or positive result would then be subject to scalpel biopsy for a definitive diagnosis.

Scuibba (1999) reported that the brush biopsy shows promise, particularly for Class I lesions.[33] Permission to administer a brush biopsy

varies by state, so hygienists must consult with their governing board to determine whether this test falls within their scope of practice.

Saliva Testing

Saliva testing for genetic patterns linked with oral cancer is an emerging area of research. Four specific patterns of messenger RNA, identified by a research team at the University of California, Los Angeles, appeared in the saliva of patients with oral squamous cell carcinomas. The team created an assay that pinpointed those mRNAs with 91% accuracy, and sensitivity and specificity was comparable or better than blood samples.[34] To date, the saliva-based testing has not been incorporated into a commercial product, but researchers are hopeful that the technology will come to the marketplace. The Oral Fluid NanoSensor Test (OFNASET) Cartridge is a hands-free, disposable, "lab-on-a-chip" currently being tested at UCLA for saliva-based oral cancer diagnostics.[35]

Conclusion

The realm of oral cancer detection adjuncts and tests is an exciting and constantly progressing area of research and technology. Detection tools are becoming increasingly accurate and less invasive as studies continue to be published in order to determine the sensitivity and specificity of each detection mechanism. Instructional and educational materials as well as supporting information on how they can be best utilized in your practice are essential for success.

As healthcare providers, dental hygienists play a vital role in their patients' oral and overall health. As licensed health professionals, all team members in dentistry must realize that it is important to have an awareness of the cutting edge research, and to be prepared to apply current chairside detection techniques as part of our routine treatment. Early detection of oral cancer is the key to survival, and an oral cancer exam is essential for each patient every time they enter the dental office. Integration of the adjuncts and tests discussed here can help uncover hidden lesions before they have the chance to progress into malignancy, and hopefully improve patients' chances of living a long, healthy life.

About the Authors

Tricia Osuna, RDH, BS, FAADH, is a USC graduate and President of the American Academy of Dental Hygiene. Tricia has over 30 years of experience as a dental hygienist to share with her audiences in a humorous, enlightening and participatory presentation experience. Ms. Osuna is a lifelong CDHA/ ADHA member and a previous Member of the Dental Board of California. Licensed in both California and New York, her experiences traverse the dental hygiene arena in a very unique way. Tricia's career spans a variety of roles in the profession of dental hygiene including Consultant, Clinician, Educator, Author, Mentor as well as business owner and President of Professional Insights, Inc.

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Please Note!

References available upon request and
in the online version of this CE.
Go to:
www.cdha.org
click on the Education & Online CE section
for a full reference list.

LifeLongLearning References

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Home Study Correspondence Course

"Oral Cancer Diagnostic Technologies"

Tricia Osuna, RDH, BS
Suzie Hopkins, BA

2 CE Units – Member $25, Potential member $35

Circle the correct answer for questions 1-10

1. The most common oral cancers are squamous cell carcinomas.
   a. True b. False
2. Of those newly identified with oral cancer, 50% will not live past five years after initial diagnosis.
   a. True b. False
3. The patient populations with the highest risk for oral cancer do not include people who:
   a. have a history of oral cancer.
   b. are 30 and under.
   c. use tobacco and alcohol.
   d. have premalignant lesions or dysplasia.
4. The area of highest incidence of oral squamous cell carcinoma are located where?
   a. Tongue
   b. Lower Lip
   c. Floor of mouth
   d. Oropharynx/soft palate
5. Early detection is the key to decreasing both morbidity and mortality associated with Stage I and II squamous cell carcinomas and oral premalignant lesions.
   a. True b. False
6. All listed below are types of adjunct tests or screening products EXCEPT:
   a. fluorescence.
   b. transepithelial biopsy.
   c. incandescence.
   d. chemiluminescence.
7. Chronic infections that may also be linked to heart disease and high blood pressure may be produced by the use of smokeless tobacco.
   a. True b. False
8. While alcohol alone is a risk factor, there is a dramatically increased risk of oral squamous cell carcinoma when alcohol is used in combination with which of the following?
   a. Coffee
   b. Tobacco
   c. HPV
   d. None of the above
9. Correct use of the transepithelial biopsy requires the brush to be placed against the lesion with which of the following?
   a. Light pressure and rotated 2-8 times
   b. Firm pressure and rotated 5-15 times
   c. Medium pressure and rotated 15-25 times
   d. Very firm pressure until bleeding occurs
10. Failure to diagnose oral cancer is the number two cause of dental malpractice cases.
    a. True b. False

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