Oral Cancer Today: The Impact on Our Profession

A Peer-Reviewed Publication
Written by Jo-Anne Jones, RDH

Abstract
SEER (Surveillance Epidemiology and End Results) data demonstrates a decline in oral cancer for tobacco related sites; however, there is a strong trend toward an increase in human papillomavirus (HPV) implicated sites. Due to the affinity of the virus for lymphoid tissues and posterior placement, today’s dental professional needs to be keenly aware of the subtle symptoms that accompany this newer profile. How does this affect our methods of screening for oral and oropharyngeal cancer, and is the clinical oral examination predictive of histologic diagnosis at an early stage? Two-thirds of oral squamous cell carcinomas are discovered at an advanced stage with five-year survival rates impeded significantly; 83.3% when the disease is discovered in stage I or II, and only 38% when the cancer has metastasized. This presents a call to action to elevate our knowledge regarding examination of high-risk areas and explore adjunctive screening methods to complement the traditional white light examination.

Educational Objectives:
Upon completion of this course, the dental professional will have the ability to:
1. Recognize the incidence and current etiologic factors related to oral and oropharyngeal cancer.
2. Identify subtle symptoms that may be suggestive of oral and oropharyngeal cancer.
3. Perform a visual and tactile examination of high-risk extroral and introral areas.
4. Compare and contrast the value of the clinical oral examination and adjunctive screening methods utilizing direct fluorescence visualization.

Author Profile
Jo-Anne Jones, RDH, is a well-recognized international speaker, consultant, author and successful entrepreneur. She is a Key Opinion Leader for several leading corporations within the dental community. She has been described as a very dynamic, knowledgeable and authentic speaker with an ability to powerfully communicate her knowledge. Jo-Anne proudly partners with the Oral Cancer Foundation in conveying the urgent need for changing the way in which we screen for oral cancer to meet the needs of today’s population.

Author Disclosure
Jo-Anne Jones, RDH, is a key opinion leader for DenMat Holdings, LLC.

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Abstract
SEER (Surveillance Epidemiology and End Results) data demonstrates a decline in oral cancer for tobacco related sites; however, there is a strong trend toward an increase in human papillomavirus (HPV) implicated sites. Due to the affinity of the virus for lymphoid tissues and posterior placement, today’s dental professional needs to be keenly aware of the subtle symptoms that accompany this newer profile. How does this affect our methods of screening for oral and oropharyngeal cancer, and is the clinical oral examination predictive of histologic diagnosis at an early stage? Two-thirds of oral squamous cell carcinomas are discovered at an advanced stage with five-year survival rates impeded significantly; 83.3% when the disease is discovered in stage I or II, and only 38% when the cancer has metastasized. This presents a call to action to elevate our knowledge regarding examination of high-risk areas and explore adjunctive screening methods to complement the traditional white light examination.

Incidence and Survival Rates
According to the American Cancer Society Cancer Facts and Figures 2017, it is estimated that 49,670 men and women (35,720 male and 13,950 female) will be diagnosed with cancer of the oral cavity and pharynx and 9,700 deaths are estimated.¹ Based on rates from 2011–2013 data, approximately 1.1% of men and women born today will be diagnosed with cancer of the oral cavity and pharynx at some point during their lifetime.² This number can also be expressed as 1 in 90 men and women will be diagnosed with cancer of the oral cavity and pharynx during their lifetime.

This is the ninth year in a row in which there has been an increase in the rate of occurrence of oral and oropharyngeal cancer. In 2007, there was a major jump of over 11% in that single year. In 2013, there was an estimated 300,682 people living with oral cavity and pharynx cancer in the United States.² Worldwide, the problem is far greater. Oral and oropharyngeal cancer, grouped together, comprise the sixth most common cancer in the world. In certain high-risk southeast Asian countries such as Sri Lanka, India, Pakistan, and Bangladesh, oral cancer is the most common cancer in men and may contribute up to 25% of all new cases of cancer.³ Many different factors predispose countries such as India to high incidence rates of oral and oropharyngeal cancer. Risk factors in these countries include alcohol, tobacco, smokeless tobacco products, betel nut chewing, and the human papillomavirus (HPV).⁴

The median age at diagnosis for both HPV⁶ and non-HPV⁵ cancers of the oral cavity and oropharyngeal area is 62, representing both primary etiologic pathways. Five-year relative survival rates for all stages of the oral cavity and pharynx are 63% as illustrated by Table 1.⁸ This represents an increase in survival rates when compared to previous years. This is primarily due to an increase in HPV-related cancers, which are more sensitive and responsive to treatment, resulting in a significant survival advantage accompanied by a profile of otherwise healthy, young males. “Published data indicate that tumor HPV status is a strong and consistent determinant of superior survival, regardless of treatment strategy, with 5-year survival rates among patients with HPV-positive tumors of approximately 75 to 80%, versus 45 to 50% among patients with HPV-negative tumors.”⁹ The subset of HPV-related cancers is the fastest growing segment of the oral and oropharyngeal cancer population. White, nonsmoking males age 35–55 are most at risk, with a gender predisposition of 4 to 1 over females.¹⁰ The survival statistics presented in Table 2 were tabulated between 2006 and 2012¹⁰ and are based on the stage of discovery of the oral and oropharyngeal cancer.¹¹

Review of Etiologic Factors
Tobacco and tobacco products, alcohol, prolonged sun exposure, betel nut chewing, use of areca nut, cannabis use, previous history of oral cancer, and HIV seropositivity along with predisposing factors such as age, gender, socioeconomic status, and genetics are all cited as risk factors for oral cancer. It is, however, the human papillomavirus (HPV) that has captured the attention of the medical and dental communities as the fastest growing etiologic factor. “The increase in incidence of HPV-positive OPSCC [oropharyngeal squamous cell carcinoma] is epidemic, and OPSCC will likely soon be the most common cancer in the United States caused by HPV as well as the most common cancer of the upper aerodigestive tract. Patients with HPV-positive OPSCC are more likely to be white, middle-aged, of moderate to upper income, and to have had more oral sexual partners.”¹² “Local-regional metastasis, but not distant metastasis, was significantly lower for patients with HPV-positive tumors than for those with HPV-negative tumors. In addition, cumulative incidence of second primary tumors was significantly lower among patients with HPV-positive tumors, largely because of lower rates of smoking related cancer.”¹³

The vast majority of oropharyngeal cancers are HPV-associated cancers with 60% being attributed to specific high-risk viral strains of HPV 16 and 18. https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-factsheet These are the same two strains that comprise the majority of HPV-related cervical cancers. Ninety-one percent of oropharyngeal cancers are attributed to viral strains 31/33/45/52/58 and other types.¹⁴
Table 1. Age Distribution (%), Median Age at Diagnosis, 5-year Relative Survival, and Estimated Number of New Cases by Cancer Type

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Median age at diagnosis</th>
<th>Estimated new cases, 2016</th>
<th>5-year relative survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>65</td>
<td>1,685,210</td>
<td>67%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>73</td>
<td>76,960</td>
<td>77%</td>
</tr>
<tr>
<td>Gallbladder*</td>
<td>72</td>
<td>11,420</td>
<td>18%</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>71</td>
<td>18,960</td>
<td>82%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>71</td>
<td>53,070</td>
<td>7%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>70</td>
<td>224,390</td>
<td>17%</td>
</tr>
<tr>
<td>Myeloma</td>
<td>69</td>
<td>30,330</td>
<td>47%</td>
</tr>
<tr>
<td>Stomach</td>
<td>69</td>
<td>26,370</td>
<td>29%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>68</td>
<td>134,490</td>
<td>65%</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>67</td>
<td>19,950</td>
<td>26%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>67</td>
<td>16,910</td>
<td>18%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>66</td>
<td>72,580</td>
<td>70%</td>
</tr>
<tr>
<td>Prostate</td>
<td>66</td>
<td>180,890</td>
<td>99%</td>
</tr>
<tr>
<td>Larynx</td>
<td>65</td>
<td>13,430</td>
<td>61%</td>
</tr>
<tr>
<td>Small intestine</td>
<td>65</td>
<td>10,090</td>
<td>66%</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>64</td>
<td>8,220</td>
<td>63%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>64</td>
<td>8,220</td>
<td>63%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>63</td>
<td>39,230</td>
<td>17%</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>63</td>
<td>76,380</td>
<td>92%</td>
</tr>
<tr>
<td>Ovary</td>
<td>63</td>
<td>22,280</td>
<td>46%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>62</td>
<td>48,330</td>
<td>63%</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>62</td>
<td>60,050</td>
<td>83%</td>
</tr>
<tr>
<td>Breast (Female)</td>
<td>61</td>
<td>246,660</td>
<td>89%</td>
</tr>
<tr>
<td>Eye &amp; orbit</td>
<td>61</td>
<td>2,810</td>
<td>82%</td>
</tr>
<tr>
<td>Soft tissue (including heart)</td>
<td>59</td>
<td>12,310</td>
<td>65%</td>
</tr>
<tr>
<td>Brain &amp; other nervous system</td>
<td>58</td>
<td>23,770</td>
<td>33%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>50</td>
<td>64,300</td>
<td>98%</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>49</td>
<td>12,990</td>
<td>68%</td>
</tr>
<tr>
<td>Bones &amp; joints</td>
<td>42</td>
<td>3,300</td>
<td>97%</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>38</td>
<td>8,500</td>
<td>86%</td>
</tr>
<tr>
<td>Testis</td>
<td>33</td>
<td>8,720</td>
<td>95%</td>
</tr>
<tr>
<td>Acute lymphocytic leukemia</td>
<td>14</td>
<td>6,590</td>
<td>68%</td>
</tr>
</tbody>
</table>

*New case estimate includes other biliary. Note: Cancer types are ranked in descending order of median age at diagnosis. Sources: Age distribution based on 2011-2012 data from the North American Association of Central Cancer Registries and excludes incidence data from Arkansas and Nevada. Median age at diagnosis and 5-year relative survival are based on cases diagnosed during 2008-2012 and 2005-2011, respectively, from the 18 SEER registries and were previously published in the SEER Cancer Statistics Review, 1975-2012. 2016 estimated cases from Cancer Statistics, 2016. American Cancer Society, Surveillance and Health Services Research, 2016.

Table 2. Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Oral Cavity and Pharynx Cancer

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>Stage Distribution</th>
<th>5-Year Relative Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized (confined to primary site)</td>
<td>30%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Regional (spread to regional lymphnodes)</td>
<td>47%</td>
<td>63.3%</td>
</tr>
<tr>
<td>Distant (cancer has metastasized)</td>
<td>18%</td>
<td>38.0%</td>
</tr>
<tr>
<td>Unknown (unstaged)</td>
<td>5%</td>
<td>47.2%</td>
</tr>
</tbody>
</table>

HPV has an affinity for the tissue of the oropharynx, most notably the base of the tongue and the lingual and palatine tonsils. Surveillance data indicate that incidence of tongue and tonsillar cancers increased steadily between 1973 and 2007, whereas rates of cancers at other oral and pharyngeal sites decreased. Results from a study published more recently whereby investigators examined the HPV status of 271 patients with oropharyngeal cancer from three SEER sites showed that the incidence of HPV-positive cancers increased by 225% during 1988 through 2004; whereas the incidence of HPV-negative cancers decreased by 50% during the same period as illustrated by Table 4.

Table 3. Number of HPV-Associated and HPV-Attributable Cancer Cases per Year

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Average number of cancers per year in sites where HPV is often found (HPV-associated cancers)</th>
<th>Percentage probably caused by any HPV type</th>
<th>Number probably caused by any HPV type</th>
<th>Percentage probably caused by HPV types 16/18</th>
<th>Number probably caused by HPV types 31/33/45/52/58</th>
<th>Percentage probably caused by HPV types 31/33/45/52/58</th>
<th>Number probably caused by HPV types 31/33/45/52/58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>11,771</td>
<td>91%</td>
<td>10,700</td>
<td>66%</td>
<td>7,800</td>
<td>15%</td>
<td>1,700</td>
</tr>
<tr>
<td>Vagina</td>
<td>802</td>
<td>75%</td>
<td>600</td>
<td>55%</td>
<td>400</td>
<td>18%</td>
<td>100</td>
</tr>
<tr>
<td>Vulva</td>
<td>3,554</td>
<td>69%</td>
<td>2,400</td>
<td>49%</td>
<td>1,700</td>
<td>14%</td>
<td>500</td>
</tr>
<tr>
<td>Penis</td>
<td>1,168</td>
<td>63%</td>
<td>700</td>
<td>48%</td>
<td>600</td>
<td>9%</td>
<td>100</td>
</tr>
<tr>
<td>Anus</td>
<td>5,010</td>
<td>91%</td>
<td>4,600</td>
<td>79%</td>
<td>4,000</td>
<td>8%</td>
<td>400</td>
</tr>
<tr>
<td>Female</td>
<td>3,260</td>
<td>93%</td>
<td>3,000</td>
<td>80%</td>
<td>2,600</td>
<td>11%</td>
<td>400</td>
</tr>
<tr>
<td>Male</td>
<td>1,750</td>
<td>89%</td>
<td>1,600</td>
<td>79%</td>
<td>1,400</td>
<td>4%</td>
<td>100</td>
</tr>
<tr>
<td>Rectum</td>
<td>750</td>
<td>91%</td>
<td>700</td>
<td>79%</td>
<td>600</td>
<td>8%</td>
<td>100</td>
</tr>
<tr>
<td>Female</td>
<td>513</td>
<td>93%</td>
<td>500</td>
<td>80%</td>
<td>400</td>
<td>11%</td>
<td>100</td>
</tr>
<tr>
<td>Male</td>
<td>237</td>
<td>89%</td>
<td>200</td>
<td>79%</td>
<td>200</td>
<td>4%</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>15,738</td>
<td>70%</td>
<td>11,000</td>
<td>60%</td>
<td>9,500</td>
<td>6%</td>
<td>900</td>
</tr>
<tr>
<td>Female</td>
<td>3,100</td>
<td>63%</td>
<td>2,000</td>
<td>51%</td>
<td>1,600</td>
<td>10%</td>
<td>300</td>
</tr>
<tr>
<td>Male</td>
<td>12,638</td>
<td>72%</td>
<td>9,100</td>
<td>63%</td>
<td>8,000</td>
<td>4%</td>
<td>600</td>
</tr>
<tr>
<td>TOTAL</td>
<td>38,793</td>
<td>30,700</td>
<td>24,600</td>
<td>3,800</td>
<td></td>
<td></td>
<td>3,800</td>
</tr>
</tbody>
</table>

*HPV types detected in genotyping study; most were high-risk HPV types known to cause cancer (Saraiya M et al. US assessment of HPV types in cancers; implications for current and 9-valent HPV vaccines. Journal of the National Cancer Institute 2015;107;djv086).*

How is HPV connected to oral and oropharyngeal cancer? Currently the human papillomavirus is the most common sexually transmitted infection (STI) in the United States. “HPV is so common that nearly all sexually active men and women get it at some point in their lives.” The Annual Report to the Nation on the Status of Cancer (1975–2009), featuring the burden and trends in HPV-associated cancers and HPV vaccination coverage levels provides an update of cancer incidence (new cases) and mortality (death) rates and trends in the United States. A special feature section for the 2013 report compiled by the American Cancer Society (ACS), Centers for Disease Control and Prevention (CDC), and the North American Association of Central Cancer Registries (NAACR) highlighted the burden and trends in HPV-associated cancers.

Cervical cancer is the most common HPV-associated cancer among women, and oropharyngeal cancers (cancers of the back of the throat, including the base of the tongue and tonsils) are the most common among men as illustrated in Table 3. Overall prevalence included both low-risk and high-risk HPV types. Low-risk types of HPV can cause genital warts or other nonmalignant conditions. The oncogenic transformation of HPV to oropharyngeal cancer is related to a persistent infection with a high-risk strain such as p16. This change in etiology apparent over the last two decades has greatly influenced the demographics of today’s oral and oropharyngeal cancer patient. The virally transmitted disease is affecting younger patients, predominantly males who often have never used tobacco products, and the disease lay hidden and dormant for many years. The global increase in HPV-oropharyngeal cancer has been tied in with sexual relations, namely oral sex as the most common transmission vector.
“A high number of lifetime vaginal and oral sexual partners, young age of onset of sexual activity, history of anogenital warts in men may be a potential source of viral colonization of the oral mucosa. However, patients with oropharyngeal SCC (squamous cell carcinoma) and higher numbers of sexual partners constitute only a small part of head and neck squamous cell carcinoma patients. Therefore, a low number of sexual partners does not exclude the diagnosis; husbands [partners] of women with in-situ and invasive cervical cancer, patients with a history of HPV-associated anogenital cancers, immunocompromised individuals (post-transplant patients and HIV infected ones) are also at high risk of developing HPV-associated HNSCC (head and neck squamous cell carcinoma).”

Early Recognition of Subtle Symptoms
Often patients do not seek medical attention until tumors are large enough to cause symptoms as small tumors typically cause little distress. Health-care professionals need to recognize that oral cancer does not always occur in people who smoke, use tobacco products, and consume alcohol. Many patients seek medical care with symptoms of head and neck cancer for many months prior to diagnosis. Clinical manifestation may be limited to a swelling in the neck or a recurrent sore throat, repeatedly treated with antibiotics with no resolution.

There are a number of subtle symptoms that accompany HPV-related oropharyngeal cancer that dental professionals need to be aware of as well as those associated with oral cancer. All of these symptoms share a commonality of being persistent and not resolving. Symptoms include, but are not limited to, the following:
- Hoarseness
- Continuous sore throat or a throat infection not responding to antibiotics
- Asymmetry in the tonsillar area
- Pain when swallowing or difficulty swallowing (dysphagia)
- Expectoration of blood (hemoptysis)
- Pain when chewing
- Continental lymphadenopathy
- Nonhealing oral lesions
- Unilateral ear pain
- A lump in the throat or the feeling that something is stuck in the throat
- Unexplained weight loss
- Tongue that tracks to one side when stuck out

Dental patients should be encouraged to conduct a self-examination of their head and neck as well as intraoral structures at regular intervals. This activity in itself will assist in earlier discovery of an abnormal mucosal or extraoral finding. Patients should be instructed to watch out for any of the above as well as:
- A lump or thickening in the mouth, neck or face
- Indurations or hard spots on the tongue, particularly on lateral borders
- A fixed, hard, and painless lump on the neck that has been present for over two weeks

Examination of High-Risk Areas
The most common sites for HPV-related oropharyngeal cancer are the base of the tongue, the oropharyngeal area, tonsils, and tonsillar pillars. Smoking and alcohol related oral cancer, in contrast, tend to involve the anterior portion of the tongue, lateral borders, floor of mouth, and the palate.

The visual access of these areas is limited, making detection at any earlier stage somewhat compromised. Optimal visual acuity is of utmost importance. The use of magnification with customized loupes is of great benefit when conducting a thorough and effective extraoral and intraoral examination. Innovations in design and function offer today’s dental professional many choices for improved visual acuity through the use of magnification and lighting. (Figures 1 and 2) Throat Scope® is the world’s first all-in-one illuminated tongue depressor, which assists in depressing the tongue to gain superior visual access to the posterior areas of the oropharynx as well as illuminating high-risk anatomical areas that are often difficult to access. (Figure 3) Throat Scope® also provides direct illumination in order to effectively facilitate an oral self-examination. (Figure 4)
A review and assessment of the systemic health, risk factors, and pharmacological status of the patient is always done prior to the extraoral and intraoral examination. Following the accumulation of this data, a systematic examination of the head, face, and neck should be conducted, including the temporomandibular joint, masseter muscle, parotid gland, frontal and maxillary sinuses, and palpation of the thyroid gland. There are a number of areas that are considered high risk and more vulnerable to oral and oropharyngeal cancer. A thorough and effective examination of the lymph nodes is critical in the early identification of an abnormal lesion or growth. The lymph nodes are examined with the clinician positioned behind the patient with the patient sitting upright in the dental chair. It is important to employ a systematic approach to the examination. A suggested order would be to commence with palpation of the submental and submandibular glands followed by the cervical nodes (deep and superficial), supraclavicular, occipital, post- and preauricular nodes.

Palpation of the lymph nodes is accomplished with fingertips exerting firm pressure. When examining the submental nodes, instruct the patient to bite together lightly and place the tongue into the palatal vault. This results in tensing of the mylohyoid muscle, facilitating easier palpation of submental glands. (Figure 5)

The submandibular glands are again a critical area with afferent and efferent drainage pathways linked to upper respiratory infections, mononucleosis, mycobacterial infections, oral disease, as well as squamous cell carcinomas of the head and neck. They are best examined with firm, unilateral palpation following a cursory bilateral palpation. Once fingers are in position, instruct the patient to place their chin down and ear over to the shoulder of the side being palpated. This facilitates deep palpation of the nodes. (Figure 6)
Next is the palpation of the cervical nodes. This set forms a complex chain of numerous nodes that drain the larynx, tongue, oropharynx, and anterior neck. Landmark the sternocleidomastoid muscle (SCM), which is a bilateral muscle found in the superficial layers of the side of the neck dividing the neck into anterior and posterior triangles. It is one of the largest and most superficial cervical muscles originating at the clavicle with an insertion at the mastoid process of the temporal bone of the skull. With four fingers positioned along the anterior aspect of the SCM, palpate the superficial cervical lymph nodes along the full length of the muscle. Palpate the deep cervical nodes by instructing the patient to turn their head in the opposite direction in order to reposition the sternocleidomastoid muscle for better access to the deeper nodes. (Figure 7) At the same time, palpate the posterior cervical nodes.

The supraclavicular nodes are palpated next. They are positioned superior to the clavicle in the hollow area or supraclavicular fossa directly above the collarbone. They drain a portion of the thoracic cavity, gastrointestinal tract, and genitourinary tract. Supraclavicular node enlargement is the most worrisome. “Supraclavicular lymphadenopathy has the highest risk of malignancy, estimated as 90 percent in patients older than 40 years and 25 percent in those younger than age 40.”

An enlarged node may be the first indicator of a thoracic or abdominal neoplasm, thyroid or laryngeal disease, or mycobacterial/fungal infection. Deeper palpation may be accomplished by having the patient lower their chin, raise their shoulders, and round shoulders forward.

The next nodes to be palpated are the occipital nodes. These are associated with the occipital artery at the posterior base of the skull. Using a bilateral technique, palpation is done directly below the base of the occipital bone. Repositioning the patient’s head to the front, exposing the occipital area may facilitate better access for palpation of the occipital nodes.

The posterior auricular, or postauricular, nodes are next in the systematic order of lymph node palpation, and are usually two in number. The anterior auricular or preauricular nodes are from one to three in number and lie immediately in front of the tragus (the projection of skin covered cartilage of the external ear). Both pre- and postauricular nodes efferent vessels drain into the superior deep cervical nodes.

In the broadest clinical terms, the enlarged node, if related to infection, is most often soft, freely movable, and painful. Also, the patient may have presented with an infection (or presence of inflammation) and may possess some knowledge of the etiology. Malignant neoplasm related nodes are normally fixed, particularly in the later stages, and they are generally not painful. One could compare the consistency of an infection related node to a blueberry or pea, whereas a malignant neoplasm related node is normally firmer in consistency, like a stone.

The intraoral anatomical structures that present a high degree of vulnerability are the tongue, floor of the mouth, palatal tissues, and the oropharyngeal area. Again, it is imperative to conduct a thorough and systematic examination of all areas of the oral cavity and oropharyngeal area including:

- Lips
- Labial mucosa
- Buccal mucosa
- Gingival tissues
- Tongue
- Floor of mouth
- Oropharyngeal and palatal tissues

The tongue should be examined using both visual and tactile methods. Visual inspection alone is inadequate to detect early mucosal changes. The dorsum of the tongue is the first area to be examined. Instruct the patient to first stick out their tongue, then move their tongue from side to side noting any abnormality or restriction. A clinical consideration to note is that the lack of ability to do this may be a subtle sign of a mass at the base of the tongue restricting full movement. With the patient’s tongue at rest, and mouth partially open, inspect and palpate the dorsum of the tongue to detect any swelling or fixed mass.

Following inspection of the dorsum, examine the lateral borders. A common site for oral cancer is on the lateral aspect of the tongue. With retraction of the cheek, inspect the left and right lateral margins of the tongue. Handling the tip of the tongue with a piece of gauze will assist full protrusion and will aid examination of the more posterior aspects of the tongue’s lateral borders, including the lingual tonsils. (Figure 8) With the tongue fully protruded (held and manipulated forward and side to side by the clinician for optimal visual access), inspect the posterior aspect of the tongue using digital palpation along the lateral borders to identify any changes in tissue texture or consistency, noting any swelling or induration. If detected, compare with the opposing lateral border. Be suspicious of an abnormality that is unilateral.
The last area of the tongue to be examined is the ventral surface. Instruct the patient to touch the roof of the mouth with the tip of the tongue. This will allow full inspection of the ventral surface of the tongue. Digitally palpate the ventral surface of the tongue to aid in any detection of growths, swelling or area of tenderness, as well as any color or texture changes. Observe for any asymmetry, comparing one side to the other. (Figure 9)

Check the entire area of the oropharynx, examining the tonsillar region including the uvula, tonsillar pillars, and palatine tonsils for presence, color, and size of any abnormalities. When examining the oropharynx, it is best to depress the tongue down toward the floor of the mouth using either a tongue depressor or an all-in-one illuminated tongue depressor (Throat Scope®). The back of the mouth mirror may also be used while instructing the patient to take a deep breath in, hold and say “ah”. Even pressure dispersed over the dorsum of the tongue by a tongue depressor is less likely to stimulate the gag reflex. (Figure 3) This method enables the clinician to gain better visual access to the oropharyngeal area. The soft palate should be visually examined next, accompanied by digital palpation of the hard palate, noting any asymmetries, swelling or mucosal changes. (Figure 11)

Examine the floor of the mouth carefully, keeping in mind that this is another highly vulnerable area that requires close and thorough inspection. This area is easily hidden from visual inspection. With the tongue still elevated, inspect the floor of the mouth for changes in color, texture, swellings, or other surface abnormalities. Using bimanual palpation and consistent firm pressure, compress the floor of the mouth against the opposite hand, which is placed extraorally. (Figure 10) This is the only effective way to identify any area of firmness or mass as well as locating any feeling of tenderness.
Early Discovery of an Abnormal Lesion

As dental professionals, we possess a keen sense of identifying normal vs. abnormal tissue. If the lesion is related to trauma or injury, it is the golden rule to appoint back in 14 days to make certain the lesion has resolved. However, are we discovering oral lesions early enough? A comprehensive study based on searches of PubMed, Web of Knowledge, and the Cochrane Library from 1966 through 2010 was published in the Journal of the American Dental Association on December 1, 2012. The study was based on a systematic review to assess the effectiveness of the clinical oral examination (COE) in predicting histologic diagnosis of dysplasia and oral squamous cell carcinoma (OSCC).

The COE is the standard in practice for today’s dental clinician to determine the presence of abnormal oral mucosal changes. The practice of a COE involves a thorough visual and tactile examination of the head and neck regions and the intraoral structures and mucosa. “Relying on a COE to detect oral dysplasia and oral squamous cell carcinoma, however, may be inadequate as suggested by the finding that more than 30 percent of patients with OSCC and oropharyngeal cancer had undergone oral cancer screening during the three years before receiving a diagnosis of OSCC.” On the basis of the available literature, the authors determined that a COE of mucosal lesions generally is not predictive of histologic diagnosis. The authors conclude, “The fact that OSCCs often are diagnosed at an advanced stage emphasizes the need for improving the COE and the need to develop adjuncts to assist in oral mucosal lesion detection and diagnosis.”

Value of Adjunctive Screening Devices

When lesions are found that are highly suspect, the need for a referral becomes evident. When an etiologic factor is identified, it is either removed (e.g., a restoration that is causing tissue trauma) or the patient is followed up in two weeks to reevaluate to be certain the lesion has resolved. If an etiologic factor cannot be identified, the management pathway is either to refer immediately or at the very minimum to follow up in two weeks pending the subjective and objective assessment of the abnormal lesion.

There are a number of adjunctive screening technologies that are available and continue to emerge in the dental marketplace. It is important to recognize that adjunctive screening technologies can provide valuable additional information (beyond the visual and tactile examination process) for further evaluation and assessment.

Vital staining of a visible mucosal lesion using pharmaceutical grade 1% toluidine chloride or toluidine blue (referred to as TBlue) is an adjunctive aid as a tissue marker that has been utilized for more than 40 years. TBlue is applied to the tissue and then decolorized. The decolorization is done with reapplication of the acetic acid. The dye has an affinity for nuclear material with a high DNA or RNA content that supports its selective concentration in dysplastic or malignant cells within the oral epithelium.

The brush test provided by OralCDx (www.thebrushtest.com) is part of the diagnostic process rather than the discovery process, as it examines an already visible clinical finding. Cells are collected from the visible lesion and sent for further investigation. The results obtained guide the clinician as to the requirement for a scalpel biopsy to investigate the area further. A positive result must be followed with a full-thickness biopsy (incisional or excisional) in order to determine the extent and nature of the disease process. A study published in Head and Neck Oncology was the first of its kind where oral brush and scalpel biopsies were performed simultaneously on patients with minimally suspicious oral lesions. The results of the computer-assisted analysis indicated that the brush biopsy was a highly sensitive and noninvasive test that can be used to evaluate oral lesions that appear clinically benign or without the identification of an etiology.

By the time we discover the lesion and its clinical manifestation, it is often too late or in the more advanced stages. Abnormal cellular differentiation begins at the basement membrane, making earlier discovery with white light examination extremely challenging or nonexistent. Direct fluorescence visualization, also referred to as narrow-band light imaging or FV, has been well studied. Direct fluorescence visualization works on the premise of the ability of human tissue to fluoresce due to naturally occurring fluorophores in oral mucosa under excitation with a specific wavelength and intensity of light. By utilizing special optical filters, the clinician is able to immediately view different fluorescence patterns in the oral tissue to help differentiate between normal and abnormal cellular activity that would otherwise not be visible with white light examination. (Figures 12 and 13) VElscope Vx, a leader in direct fluorescence visualization, utilizes proprietary filtering of the fluorescence light to optimize the contrast between normal and abnormal tissue.

Figure 12. Oropharyngeal tissues examined under white light
As dysplasia begins to develop, there is a breakdown in the stroma and specifically in the connective tissue or collagen cross-links coupled with a reduction in the naturally occurring fluorophores, greatly diminishing the ability of the tissue to fluoresce. This allows for real-time feedback of an irregular dark area which may not have been present under white light examination, presenting a stark contrast to the surrounding tissue that appears as an apple green glow. (Figures 14-17)

Figure 14. Nonevident lesion under white light examination

Figure 15. Irregular, well-demarcated loss of fluorescence visible with direct fluorescence examination (VELscope); biopsy confirmed carcinoma-in-situ

Figure 16. Lateral border of the tongue demonstrating a mixed leukoplakic/erythroplakic lesion under white light examination

Figure 17. Irregular, well-demarcated and defined extent of lesion visible with VELscope Vx system; biopsy confirmed severe dysplasia
The Science Supporting Fluorescence Visualization

A clinical study published in General Dentistry, July/August 2011, by Truelove et al. examined 620 low-risk patients with loss of fluorescence suggestive of pathology in 69 subjects or 11.1%. After a second immediate evaluation, 28 of the 69 subjects were scheduled for follow-up. None of the lesions discovered in these 28 subjects, which included five dysplasias, had been detected using standard white light examination. Thus, adjunctive use of this technique led to the earlier discovery of histologic changes. The conclusive statement was that adding an adjunctive diagnostic procedure such as direct fluorescence visualization improved the quality and outcome of the examination process.

A study conducted by Laronde et al. examined the value of using direct fluorescence visualization (VELscope system) as an aid in decision making when screening for oral lesions including oral cancer. “One of the most difficult decisions a clinician may face is when to refer a lesion for further investigation and biopsy.” The outcome of the oral cancer screening examination is solely dependent on the knowledge and experience of the clinician. The methods involved training the dentists in a systematic manner to conduct the medical history, head and neck evaluation including the oral exam, and the use of direct fluorescence visualization (FV) as an adjunctive screening tool. Using the lesion risk assessment criteria, lesions were grouped into low, intermediate, or high risk, and then FV status was determined. The results of the study revealed that the most predictive model for lesion persistence included both the use of direct fluorescent visualization accompanied by a lesion risk assessment. This provided proof of principle that the use of direct fluorescent visualization is a valuable component to oral lesion evaluation.

The results of a study led by Dr. Catherine F. Poh et al. examined the efficacy of FV (fluorescence visualization) guided surgery in reducing loco-regional recurrence and improving overall survival. The results of the study were subsequently published in the Journal of the American Medical Association in January 2016. The case-control observational study was conducted from September 1, 2004, to August 31, 2009, involving 246 patients aged 18 years of age or older who had undergone curative surgical treatment of a high-grade oral lesion (severe dysplasia, carcinoma in situ, or squamous cell carcinoma < 4 cm). All subjects had at least one follow-up visit. One hundred fifty-four patients underwent surgery with the guidance of fluorescence visualization, and 92 had conventional surgery and comprised the control group. Among the 156 patients with squamous cell carcinoma, 92 who were in the FV group demonstrated significant reduction in the three-year local recurrence rate, compared to the control group (40.6% to 6.5% in FV group) representing six of the 92 patients. Among the 90 patients with high-grade lesions, 62 who were in the FV group demonstrated a reduction in local recurrence when compared to the control group (39.3% to 8.1% in FV group). The study concluded that using FV as part of the surgical margin decision-making significantly reduced the rate of local recurrence in both early and pre-invasive stage oral cancers.

The most common misunderstanding is the reported occurrence of false positives. This notion typically arises when an adjunctive device is incorrectly treated as if it were a diagnostic test with a well-defined positive or negative outcome. This is no truer of the adjunctive procedure than it is of the COE itself. The gold standard for histologic diagnosis is excisional biopsy. It is critical to recognize that adjunctive devices such as VELscope Vx, OralID, and Identifi, etc. are not stand-alone diagnostic devices or tests. They are simply screening tools to enhance our ability to discover oral abnormalities at the earliest stage possible.

There are a few simple interpretation principles when employing the use of fluorescence visualization.

- Is there bilateral symmetry? If so, it is likely a normal anatomical landmark.
- Be aware of a unilateral presentation as opposed to a bilateral one.
- Be especially careful about a nonsymmetrical lesion with an irregular and/or well-delineated border; this is a warning sign.
- Both melanin and blood will absorb light, resulting in a marked decrease in fluorescence.
- Blood may be differentiated by employing diascopic pressure (testing for blanchability of tissue employing pressure). Blood will be displaced, resulting in tissue blanching.
- Keratin is a structural protein that fluoresces strongly when excited by blue light.
- Areas of chronic, repeated irritation such as linea alba will show up bright white.
- Porphyrin is produced by bacteria and fluoresces quite strongly when excited by blue light and shows up bright red/orange color.

When looking at the integration of an adjunctive screening device, make certain the device is supported by device-specific research. The ability to obtain images via seamless acquisition is also critical to meet the needs of reevaluation or the requirement to send to a specialist for referral management. Last but not least, does the manufacturer provide comprehensive training on how to interpret findings? Training is critical for the elimination of unnecessary and unwarranted specialist referrals.
Regardless of what adjunctive strategies we employ, all persistent lesions require evaluation and never “watchful waiting.” Failure to investigate further can result in advanced stage discovery, more complex treatment protocols, compromised quality of life, and even death.

Summary

The value in opportunistic screening has been proven time and again. First and foremost, all adult patients should receive a comprehensive extraoral and intraoral examination at least annually.

With the acquired knowledge of risk behaviors and prevention strategies, our profession is strategically positioned to play an integral role in earlier discovery of an abnormal lesion. The impact of earlier discovery is far reaching and one of the most gratifying aspects of our profession.

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Acknowledgement

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Author Profile

Jo-Anne Jones, RDH, is a well-recognized international speaker, consultant, author and successful entrepreneur. She is a Key Opinion Leader for several leading corporations within the dental community. She has been described as a very dynamic, knowledgeable and authentic speaker with an ability to powerfully communicate her knowledge. Jo-Anne proudly partners with the Oral Cancer Foundation in conveying the urgent need for changing the way in which we screen for oral cancer to meet the needs of today’s population.

Author Disclosure

Jo-Anne Jones, RDH, is a key opinion leader for DenMat Holdings, LLC.
Questions

1. Which of the following statements is correct?
   a. Oral cancer is the sixth most common cancer worldwide
   b. Yearly incidence is in excess of 400,000 cases
   c. Slightly more than half of those diagnosed today will survive more than five years
   d. All of the above statements are correct

2. The five-year relative survival rate for oral and oropharyngeal cancer is 63%, which is lower than the following cancer(s):
   a. Breast cancer
   b. Prostate cancer
   c. Uterine cancer
   d. All of the above

3. Which of the following has been identified as the fastest growing etiologic factor related to oral and oropharyngeal cancer?
   a. HIV sero-positive
   b. Human papillomavirus (HPV)
   c. Herpes simplex virus (HSV)
   d. Acquired immunodeficiency syndrome (AIDS)

4. Opportunistic oral cancer screening is best represented by:
   a. Performing an extraoral/intraoral examination on all adult dental patients annually
   b. Performing an extraoral/intraoral examination on all patients over the age of 40
   c. Performing an intraoral examination on all adult patients who smoke
   d. Performing an extraoral examination on all adults who are sexually active

5. Which of the following statements applies to late-stage discovery of oral cancer?
   a. Distant oral and oropharyngeal cancer has a 60% five-year relative survival rate
   b. Localized oral and oropharyngeal cancer has an 83% five-year relative survival rate
   c. Both of the above statements are correct
   d. Both a and b are incorrect

6. Identify the following statement which applies to the human papillomavirus:
   a. The majority of oropharyngeal cancers are HPV-associated
   b. 60% of HPV-positive oropharyngeal cancers are attributed to specific high-risk viral strains, i.e., HPV-16 and 18
   c. Both of the above statements are correct
   d. Both a and b are incorrect

7. The human papillomavirus (HPV) may be transmitted by:
   a. Oral sex
   b. Open-mouthed kissing
   c. Vaginal intercourse
   d. All of the above statements are correct

8. A sore in the mouth presenting abnormal color or texture should be managed as follows:
   a. Referral for microscopic evaluation if trauma related
   b. Referral for microscopic evaluation if etiology unknown
   c. Reapoint in 14 days if trauma related to confirm lesion has resolved. If not resolved, refer for microscopic evaluation.
   d. Both b and c apply

9. HPV has been identified as playing a dominant role in the increasing incidence of oropharyngeal cancers. Which of the following statements correctly identifies the increase?
   a. 28%-68%
   b. 225% between 1988 and 2004
   c. 80-90%
   d. None of the above is correct

10. There are a number of sites that are particularly vulnerable for oral cancer to develop. These include but are not limited to:
   a. The ventral surface of the tongue and vermilion border of the lips
   b. The tongue, palate, and floor of the mouth
   c. The buccal and labial mucosa
   d. The lips and labial mucosa

11. An enlarged or palpable node, if related to infection, is best characterized by the following:
   a. Tender to palpation
   b. Soft and moveable
   c. Fixed in position
   d. Both a and b are correct

12. A recommended systematic order of palpation of the lymph nodes is:
   a. Submental, submandibular, cervical chain (deep and superficial), supraclavicular, occipital, posterior and anterior auricular
   b. Cervical chain, supraclavicular, posterior and anterior auricular
   c. Cervical chain, supraclavicular, occipital, submental, submandibular, posterior and anterior auricular
   d. Occipital, posterior and anterior auricular, cervical chain, and supraclavicular

13. The supraclavicular nodes are palpated for the following reason(s):
   a. Lymphadenopathy in this area has the highest risk of malignancy
   b. An enlarged node may be the first indicator of a thoracic or abdominal neoplasm
   c. Drainage of part of the thoracic cavity, GI tract, and genitourinary tract
   d. All of the above are correct

14. The examination of the submandibular nodes is best accomplished by:
   a. Placing your finger pads at the angle of the mandible
   b. Using unilateral palpation and a gentle rolling stroke
   c. Firm unilateral palpation with patient’s chin down and ear to shoulder
   d. Bilateral placement of finger pads along the angle of the mandible

15. Which of the following statements is true regarding the purpose of adjunctive screening devices?
   a. Adjunctive screening devices determine histologic diagnosis
   b. An incisional/excisional biopsy is required to determine full extent and nature of disease process
   c. Adjunctive devices replace the need for scalpel biopsy
   d. Both a and b are correct

16. Which of the following adjunctive screening methods is utilized to discover what may not be visible under white light examination?
   a. Direct fluorescence visualization
   b. Indirect fluorescence visualization
   c. Oral brush biopsy
   d. Both a and b are correct

17. Which of the following data points are critical to early discovery of an abnormal lesion when using direct fluorescence visualization?
   a. Real-time feedback reveals a bilateral finding
   b. The tissue glows apple green upon inspection
   c. An irregular, dark area with a well-demarcated border that does not blanch with diascopic pressure
   d. Both b and c apply

18. The examination of the oropharyngeal area is best accomplished by:
   a. Having the patient protrude their tongue and say “ah”
   b. Depressing the tongue, having the dental patient take a deep breath in, and say “ah”
   c. Having the dental patient swallow repeatedly
   d. Having the dental patient open wide and protrude their tongue

19. A common misunderstanding is the reported “false positives” with adjunctive screening devices that provide direct fluorescence visualization. Which of the following statements addresses this misunderstanding correctly?
   a. Occurs when an adjunctive screening device is treated as a diagnostic test
   b. To be used as a screening tool only, enhancing the white light examination
   c. To enhance our ability to discover oral abnormalities at the earliest stage possible
   d. All of the above statements are correct
Questions (continued)

20. Which of the following statements refers to the efficacy of a clinical oral examination (COE)?
   a. A COE is not predictive of histologic diagnosis
   b. A COE is limited in ability to discover a lesion in the earliest stages
   c. A COE is able to provide a definitive diagnosis
   d. Both a and b are correct

21. Which of the following statements describes direct fluorescence visualization?
   a. Also called brush biopsy
   b. Is diagnostic for oral cancer
   c. Real-time feedback of naturally occurring fluorophores in human tissue
   d. Includes use of dye that has an affinity for dysplastic or malignant cells

22. Which of the following is part of the diagnostic process rather than the discovery process?
   a. Oral brush biopsy
   b. Vital staining of a mucosal lesion
   c. Direct fluorescence visualization
   d. None of the above statements are correct

23. Histologic diagnosis may only be accomplished by the following:
   a. Loss of fluorescence under excitation of a specific wavelength
   b. White light visualization
   c. Incisional/excisional full thickness biopsy
   d. None of the above statements are correct

24. Which of the following statements best describes the proper technique for examining the tongue?
   a. Visually inspect the dorsum, lateral borders, and ventral surface of the tongue
   b. Instruct the patient to stick out their tongue, move it side to side, visually inspect and palpate the dorsum, lateral borders, and ventral surface of the tongue
   c. Instruct the patient to stick out their tongue, then visually inspect and palpate the dorsum and the ventral surface
   d. Palpate the dorsum, lateral borders, and ventral surface of the tongue while it is protruded

25. HPV types 16 and 18 are:
   a. Low-risk viral strains
   b. Unrelated to cervical cancer
   c. Responsible for 25% of cervical cancers worldwide
   d. High-risk viral strains

26. Five-year survival rates differ between HPV-positive tumors and HPV-negative tumors. Which of the following statements accurately depicts this difference?
   a. 75 – 80% five-year relative survival rates among patients with HPV-positive tumors
   b. 45 - 50% five-year relative survival rates among patients with HPV-negative tumors
   c. HPV status is a strong and consistent determinant of decreased survival rates
   d. Both a and b are correct

27. Subtle symptoms that often accompany HPV-related oropharyngeal cancer include:
   a. Hoarseness
   b. Persistent sore throat or continual throat infection that does not respond to antibiotics
   c. A lump in the throat or the feeling that something is stuck in the throat
   d. All of the above are correct

28. Smoking and alcohol related oral cancers tend to involve the following anatomical area:
   a. Anterior portion of tongue, lateral borders, floor of mouth, and palate
   b. Posterior base of tongue
   c. Lingual tonsils and tonsillar pillars
   d. Base of the tongue and oropharyngeal area

29. Incidence of oral cancer may be expressed by the following:
   a. 1.1% of men and women born today will be diagnosed with oral/oropharyngeal cancer at some point during their lifetime
   b. 1 in 243 men and women will be diagnosed with oral/oropharyngeal cancer during their lifetime
   c. 1 in 90 men and women will be diagnosed with oral/oropharyngeal cancer during their lifetime
   d. Both a and c are correct

30. Bimanual palpation is required in which of the following anatomical areas?
   a. Palatal tissues
   b. Floor of the mouth
   c. Supraclavicular nodes
   d. Dorsum of the tongue

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Educational Objectives

1. Recognize the incidence and current etiologic factors related to oral and oropharyngeal cancer.
2. Identify subtle symptoms that may be suggestive of oral and oropharyngeal cancer.
3. Perform a visual and tactile examination of high-risk extraoral and intraoral areas.
4. Compare and contrast the value of the clinical oral examination and adjunctive screening methods utilizing direct fluorescence visualization.

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

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

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   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

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   5 4 3 2 1 0

9. Please rate the usefulness of the supplemental webliography.
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