It’s Time to Discuss Sex, HPV and Its Impact on Dentistry

A Peer-Reviewed Publication
Written by Lisa Dowst-Mayo, RDH, BSDH

Abstract
The new millennium has brought about great advances in technology and innovation, including the discovery of the link between human papillomavirus (HPV) and head and neck cancer. Thirty-five years ago, it was postulated that human papillomavirus could cause cervical cancer. Today, it is well established that this heterogeneous virus causes cervical, anogenital, penile and oral cancer. HPV is now considered a human carcinogen. Unlike other cancers of the mouth, HPV-positive oropharyngeal cancers are more likely to occur among younger patients, white men, those without the traditional risk factors of tobacco and alcohol and those with certain sexual histories. HPV public awareness has started to grow and has been featured more frequently in the press. As public knowledge continues to grow, so will the knowledge base of dental health care providers who treat them.

Educational Objectives
At the conclusion of this educational activity participants will be able to:
1. Perform an intraoral cancer screening to ensure all aspects of the oral cavity are evaluated.
2. Describe HPV morphology, typing and virulence and their relevance to the identification of HPV related lesions.
3. Describe how HPV is transmitted and the related oral risks for patients.
4. Make well informed decisions before purchasing enhanced oral cancer and HPV screening devices, services etc.

Author Profile
Lisa Dowst-Mayo received her Bachelor of Science degree in dental hygiene from Baylor College of Dentistry in 2002. She has been active in the tripartite of the America/Texas/Dallas & San Antonio dental hygiene associations since graduation and has held numerous leadership positions both at the state and local levels. She has worked as a full time clinical dental hygienist for the past 10 years and is currently employed at Dominion Dental Spa, the office of Dr. Tiffini Stratton DDS. She is a published author and national lecturer; you can contact her through her website at lisamayordh.com.

Author Disclosure
Lisa Dowst-Mayo has no commercial ties with the sponsors or providers of the unrestricted educational grant for this course.

Go Green, Go Online to take your course
Educational Objectives

At the conclusion of this educational activity participants will be able to:

1. Perform an intraoral cancer screening to ensure all aspects of the oral cavity are evaluated.
2. Describe HPV morphology, typing and virulence and their relevance to the identification of HPV related lesions.
3. Describe how HPV is transmitted and the related oral risks for patients.
4. Make well informed decisions before purchasing enhanced oral cancer and HPV screening devices, services etc.

Abstract

The new millennium has brought about great advances in technology and innovation; including the discovery of the link between human papillomavirus (HPV) and head and neck cancer. Thirty-five years ago, it was postulated that human papillomavirus could cause cervical cancer. Today, it is well established this heterogeneous virus causes cervical, anogenital, penile and oral cancer. HPV is now considered a human carcinogen. Unlike other cancers of the mouth, HPV-positive oropharyngeal cancers are more likely to occur among younger patients, white men, those without the traditional risk factors of tobacco and alcohol and those with certain sexual histories. HPV public awareness has started to grow and has been featured more frequently in the press. As public knowledge continues to grow, so will the knowledge base of dental health care providers who treat them.

Introduction

Think of your “ideal” high risk oral cancer patient. Did you think of a male, over 60, smoker, alcohol user, failing health with a lesion on the tongue or floor of the mouth? Or did you think of a 21 year old male or female college student, non-smoker in excellent health and weight with a lesion in the oropharynx? Both of these patients could present with oral cancer but one may be experiencing oral cancer with a connection to HPV.

There are many publications covering HPV and its probable links to dental disease. This course will discuss the lifesaving skills dentists and hygienists already possess through oral cancer screenings and how we are well-positioned to identify suspicious lesions inside the oral cavity, including those lesions which may be associated with HPV.

Oral Cavity Anatomy Review

To simplify intraoral cancer screenings, the oral cavity is divided into five main parts. By following this five-step protocol, clinicians will ensure a thorough and accurate intraoral screening, given the many structures to be viewed and palpated. It is imperative clinicians have a proficient ability to distinguish what is “typical” or “normal” from “atypical” or “abnormal.” The boundaries include: the lips demarcating the anterior boundary, the cheeks providing the lateral boundary, the palate as the superior boundary, the floor of the mouth as the inferior boundary and the back of the pharynx as the posterior boundary.

1. A good place to start is the assessment of the lips and cheeks. The clinician will want to palpate both these structures so any hard masses or tenderness can be detected. (Figure 1) From there the clinician should move to the vestibules, buccal/labial mucosa, parotid papillae, frena and lastly the gingiva (free, attached, mucogingival junction, gingival sulcus, and interdental gingiva). (Figure 2)

2. PALATE: The next areas to be observed and palpated are the hard and soft palate. If the hard palate is moveable or tender, this should be brought to the dentist’s attention as it may indicate a problem. Normal anatomy associated with the hard and soft palate includes the incisive papilla, palatine rugae, median palatine raphe and fovea. Other structures to visualize in this step are the pterygomandibular fold, retromolar pad (Figure 3) and maxillary tuberosity (Figure 4). The soft palate only makes up 15% of the palate but can be a common site for oral cancer lesions, particularly those associated with HPV. (Figure 5)

3. DORSAL/LATERAL TONGUE: Normal anatomy includes the lingual papillae (filiform, fungiform, foliate, circumvallate), median lingual sulcus, sulcus terminalis, foramen cecum, lateral borders (Figures 6, 7) and lingual

<table>
<thead>
<tr>
<th>HPV Type</th>
<th>Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV-1</td>
<td>Verruca vulgaris</td>
</tr>
<tr>
<td>HPV-2</td>
<td>Verruca vulgaris Verrucous carcinoma</td>
</tr>
<tr>
<td>HPV-4</td>
<td>Verruca vulgaris</td>
</tr>
<tr>
<td>HPV-6</td>
<td>Verrucous carcinoma Squamous papilloma Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-7</td>
<td>Oral Lichen Planus</td>
</tr>
<tr>
<td>HPV-8</td>
<td>Oral Lichen Planus</td>
</tr>
<tr>
<td>HPV-11</td>
<td>Squamous papilloma Verrucous carcinoma Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-16</td>
<td>Verrucous carcinoma Cervical, oral cancer Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-18</td>
<td>Verrucous carcinoma Cervical, oral cancer Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-31</td>
<td>Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-33</td>
<td>Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-35</td>
<td>Condyloma acuminatum</td>
</tr>
<tr>
<td>HPV-57</td>
<td>Verruca vulgaris</td>
</tr>
</tbody>
</table>
tonsils (lymph tissue on dorsal base of tongue). The base of the tongue attaches to the floor of the mouth and it is the posterior 1/3 of the tongue itself that lies in the oral aspect of the throat. (Figure 6)

4. **VENTRAL TONGUE & FLOOR OF THE MOUTH:** The ventral tongue houses deep lingual veins and plicae fimbriatae. (Figure 8) Just below the tongue are the sublingual salivary glands, lingual frenum, sublingual folds, and caruncle on the floor of the mouth. (Figure 9) It is very easy to view both structures simultaneously. Clinicians should palpate the tongue and the floor of mouth to identify any masses or hard nodules.

5. **PHARYNX (THROAT):** Separates the respiratory system from the digestive system. The pharyngeal structures can be the most challenging for clinicians to view intraorally. If a patient has a strong gag reflex or fails to say “AHHH,” these structures will not be visible as the tongue has a tendency to cover them, especially when patients are in a supine position. It only takes 5 seconds to make a patient say “AHHH” as you view the oropharynx, which could potentially save a life. Structures most visible when a patient depresses their tongue are the uvula, nasopharynx, oropharynx, fauces and palatine tonsils. (Figures 3, 10).

Below is a review of the structures associated with the pharynx.

1) **Nasopharynx:** Superior to the level of the soft palate and continuous with the nasal cavity. The pharyngeal tonsils are located in the nasopharynx which is also part of Waldeyer’s ring (definition below). Many parts are visible intraorally.

2) **Oropharynx:** Visible structures of the oropharynx are located between the soft palate and the opening of the larynx. (Figure 11)

3) **Fauces:** Openings from oral region into the oropharynx and are formed on each side by anterior and posterior tonsillar pillars and visible intraorally. (Figures 3, 10)

4) **Palatine Tonsil:** Two rounded masses between anterior and posterior tonsillar pillars on either side of the fauces. (Figure 10) This is what patients refer to as their “tonsils.” Can be visualized intraorally.

5) **Pharyngeal Tonsil:** Located on the midline of the posterior wall or roof of the nasopharynx. This tonsil is also referred to as the adenoids and will most likely not be visible intraorally.

6) **Laryngopharynx:** Inferior but close to the laryngeal opening. Not visible intraorally. (Figure 11)

7) **Epiglottis:** Cartilage that prevents food and liquid from entering the trachea. Not visible intraorally. (Figure 11)

8) **Waldeyer’s Ring:** Consists of lingual, palatine and pharyngeal tonsils. The lingual tonsils are considered a part of the base of the tongue and lie on either side of the tongue. (Figure 12)

The oral cavity is lined by a mucous membrane consisting of a stratified squamous epithelium and lamina propria made up of dense connective tissue. Keratinized tissues include the gingiva, hard palate and the dorsum of the tongue. Non-keratinized tissues are found on the lips, cheeks, vestibular fornix, alveolar mucosa, floor of mouth and soft palate. These oral tissues closely resemble the tissues of the uterine cervix, lower genital tract and skin, so it is no surprise HPV can infect them similarly. HPV-positive cancers have a preference for the oropharynx and Waldeyer’s ring as they have high levels of immature basal cells, invaginations and crypts which can harbor HPV.

**HPV Morphology, Typing & Infections**
Papillomaviruses are heterogeneous, small (52-55nm in diameter), non-segmented, double-stranded DNA genome that consists of a non-enveloped capsid.
Throughout most of the HPV lifecycle, its DNA exists in the host cell without its protein shell, having shed it during infection of the host. The virus has a special affinity for epithelial cells, namely basal cells of the dermal layer, and infects keratinocytes in a differential manner. HPV will invade the human body, sheds its protein capsid, inject its naked DNA into the cytoplasm of a healthy cell where it travels to the cell’s nucleus and replicates.

To cause malignancy, the virus will express two HPV-viral oncogenes (E6 & E7). It is through the binding of the two oncogenes to our own host proteins and inactivation of regular cell division that malignant cell growth occurs. An oncogene has the potential to cause cancer through gene mutation, environmental influence or viral infection. Many cancer drugs target these oncogenes.

HPV types are ordered in the number of their discovery and are typed by the genotypic variations in DNA base sequencing of proteins E6 and E7. Microbial virulence is due to the specific HPV proteins of E6 and E7 which is how scientists have been able to classify types as high, intermediate or low risk HPV strains. For example, the E7 protein of HPV 16 is more oncogenic than the E7 protein of HPV 8. E6 and E7 are inhibitors of tumor suppressor genes. These tumor suppressor genes interrupt cellular growth pathways that would normally lead to cell lysis and death in infected cells and are part of the body’s protection from a particular step on the pathway to cancer. If they become inhibited by E6/E7 oncogenes, destructive changes can occur more readily.

Ultimately, it is the host’s immune response that determines whether HPV persists or regresses. Since HPV does not penetrate below the basement membrane, the primary immunological exposure is to the epithelial host defense mechanisms. As long as the cell remains intact, HPV will remain unrecognized by the immune system. Trauma from friction or treatment often unMASKs the HPV from within through cell lysis. When an immune response occurs, HPV replication and change can begin to occur in the host. For example, some HPV infections are not detected by molecular testing until a woman becomes pregnant. It’s through the intense immunological and hormonal changes a woman undergoes during pregnancy that the detection of HPV was made possible.

HPV types that infect mucosal epithelia are classified as low or high risk. Low risk types cause benign oral hyperplasias that are usually painless and non-ulcerated. Most common low risk types are 6, 11, 42, 43, 44. High risk types can lead to cellular changes and cancer. Common high risk types are 16, 18, 31, 33, 35, 45, 51, 52, 56. It is not clear why certain HPV types target the skin while others target the oral mucosa or genital tract. To date, researches have positively identified 120 different strains of HPV.

Aside from oral cancer, HPV-positive infections have also been linked to many other diseases and ailments in the human body including those listed below.

1. **Verruca vulgaris:** This is also referred to as a “common wart.” It can occur on any part of the body and vary in appearance. It often appears as a raised wart with roughened surface but can also have finger-like projections that are smooth, flat, irregularly shaped or well circumscribed. The first viral positive detection was in 1982 with HPV types 2, 4 and 57 found through biopsy.

2. **Oral Lichen Planus (OLP):** When linked to the viral etiology of HPV, biopsy was able to confirm HPV types 7 and 8. OLP is thought
by some to be an autoimmune disorder involving cell-mediated cytotoxicity and destruction of the basal cells of the surface epithelium.\textsuperscript{17,18}

3. **Squamous Cell Carcinoma (SCC):** SCC is thought to be responsible for up to 95\% of all oral carcinomas.\textsuperscript{3} When SCC is found in the mouth, doctors will usually test for the presence of HPV through biopsy. Research has demonstrated that treating HPV-positive SCC versus HPV-negative can be vastly different. HPV-positive SCC treatments appear to be more responsive to chemotherapy and radiation and the survival rate is higher, having a 60-80 percent reduction in morbidity.\textsuperscript{16} There are still inconsistent reports regarding HPV and its link to SCC, but there does appear to be a strong association. It may be decades before researchers have a better understanding of this relationship.

4. **Verrucous Carcinoma (VC):** This is a variant of squamous cell carcinoma. HPV positive links were present with types 2 (17.7\%), 6/11(47\%), 16/18 (35.3\%).\textsuperscript{30} VC is defined as an uncommon exophytic low grade, well differentiated neoplasia involving the oral cavity, larynx, oropharynx, genitalia, skin and esophagus.\textsuperscript{19} It has a strong male prevalence and tends to occur around the 7th decade of life. It also has a strong association with tobacco users, particularly snuff users. When VC involves the oral cavity, it commonly arises on the buccal mucosa or lips and appears as a papillary non-ulcerated gray-white or red mass with a very broad base of attachment.\textsuperscript{19}

5. **Squamous papilloma:** Benign neoplasms with finger-like projections that resemble cauliflower and are related to HPV types 6 and 11.\textsuperscript{15} They arise from the stratified squamous epithelium of the lips, skin, oral cavity, tongue, pharynx, larynx, esophagus, cervix and/or vagina and are usually painless and do not normally lead to cancerous progression.

6. **Focal epithelial hyperplasia:** Also referred to as Heck’s disease. It is related to HPV types 13 and 32. It is found more frequently in children and HIV-positive patients. It presents as asymptomatic papules or nodules on the oral mucosa, gingiva, tongue and lips. Factors that determine disease susceptibility are unclear, but genetics and having the human lymphocytic antigen-DR4 allele in particular, are thought to play a major role in disease vulnerability.\textsuperscript{20} This condition will resolve on its own and does not appear to have long term effects.

7. **Condyloma acuminatum (CA):** Also called a venereal wart. First reported HPV particles in these lesions date back to 1976, again confirmed in 1980. CA is most commonly associated with low risk types of HPV 6 and 11. It is less commonly associated with high risk types of 16, 18, 31, 33 and 35. CA are sexually transmitted and spread by direct skin-to-skin contact during oral, genital and/or anal sex with an infected partner. Types 6 and 11 are responsible for up to 90\% of cases.

**HPV Statistics**

According to the CDC, it is estimated three out of five Americans carries at least one strain of HPV. HPV positive oral tumors were first reported in the literature in 1985. Worldwide statistics indicate that 3-5\% of adolescents and 5-10\% of adults are either infected with HPV or have experienced oral HPV-associated infection. HPV is an extremely common virus that can cause the growth of abnormal tissues or cells.

HPV is the most commonly sexually transmitted infection in the United States and it is estimated that 6.2 million individuals become newly infected each year. The CDC also reports that 5.6\% of males and females ages 14-59 have
been diagnosed with genital warts at some point in their lifetime. With more than 120 strains of HPV identified, many Americans fight the cellular changes caused by this virus. Strains 16 and 18 appear to be the most virulent. HPV16 is highly linked to cervical cancer and has been related to oropharyngeal cancer as well. Oral cancers, particularly those found in the oropharynx, have tested positive for HPV 16 and/or 18. In the United States, it is estimated that 70-90% of all cervical and oropharyngeal cancers have an HPV-positive correlation. Figure 14 shows the CDC’s most current data on cancer trends attributed to high-risk HPV infections.

HPV Transmission
HPV is transmitted by direct skin to skin contact from vaginal, anal or oral sex. Even open mouth kissing has been shown to transmit mucosal HPV strains. Most HPV infections are asymptomatic, transient and resolve on their own within 1-2 years of contraction. Most people are unaware they have contracted HPV and will show no systemic signs or symptoms. According to the CDC, 90% of low and high risk HPV infections resolve without treatment and do not always lead to cancer. Even if the virus does clear on its own, antibodies may remain and can be useful in screenings. There are other factors that may contribute to the development of cancer alongside HPV infections such as smoking, alcohol use, having multiple children, long term oral contraceptive use and HIV infections because of the immunological changes that occur systemically.

Transmission during childbirth from mother to child can occur, however, is not very common. When perinatal transmission does occur, the greatest risk for the baby is recurrent respiratory papillomatosis. It has been postulated and demonstrated in the literature that oral sex is a major culprit in this epidemic of HPV transmission. It has also been hypothesized that younger people engage in oral sex more frequently than vaginal sex due to the increased awareness and fear of HIV-transmission through vaginal and/or anal sex or the fear of pregnancy. Younger people think oral sex is safer than other forms of sex; however, no sexual activity is “safe” and without consequence. It is estimated 20-25% percent of boys and girls have had oral sex by age 15. By age 20, this percentage jumps to 75-85%. While condoms have greatly reduced the incidence of sexually transmitted disease, their effectiveness in HPV prevention is not clear; some studies even suggest condoms will not prevent HPV transmission even if used during oral sex. Many research reports are also discussing an increased risk for HPV-mediated head and neck cancers with interactions of carcinogenic substances such as alcohol, tobacco and marijuana use.

With all this information in the literature, dental professionals can no longer ignore patients’ sexual practices and histories. We need to inquire as to the HPV status of our patients in our medical histories; and if a positive response is noted then we need to ask more questions. For example:
1. Has your HPV been type-tested?
2. For women: Have you had an abnormal Pap smear result in the last 5 years?
3. Do you see your medical doctor and/or obstetrician regularly?
4. Have you ever been treated for cancer or precancerous lesions on any part of your body?

The responses to these questions may help a dental professional make better clinical decisions. For example, if a patient responds “yes” to HPV-positive status or to any of the above questions, the dental provider may want to consider salivary testing (discussed in more detail in the next section.)

Researchers have identified higher risk groups for HPV transmission including:
1. Persons who have had over twenty six vaginal sex partners in their lifetime.
2. Persons who have had more than six oral sex partners in their lifetime.
3. Persons whose first sexual encounter was at a younger age.
4. History of same sex partners.
5. Increased number of lifetime sexual partners.

HPV AND CANCER
HPV-positive oropharyngeal cancers are epidemiologically different from HPV-negative cancers. These cancers have a younger onset and are associated with high risk sexual behaviors. Head and neck cancers rank as one of the most common malignancies in the world. 90-92% are squamous cell carcinomas with 8-10% being salivary gland tumors, sarcomas or lymphomas. One recent meta-analysis confirmed HPV as an independent risk factor for oral carcinoma.

According to a literature review by Kasy et al in 2012, 30.1% of all oral squamous cell carcinomas (OSCC) had HPV prevalence. HPV-16 (25.4%) and HPV-18 (18.1%) were found in one third of all OSCC cases by detection via polymerase chain reaction of the 527 research cases reviewed. 85-95% of HPV-positive oropharyngeal cancers were caused by HPV-16 alone.

The National Cancer Institute’s information source on cancer incidence and survival is called Surveillance, Epidemiology and End Results (SEER). As reported by SEER, the incidence of oral and pharyngeal cancers has continued to rise since 2003 while other cancers of the head and neck have steadily declined. Black and white men have the highest morbidity rates. When comparing men to women of all races, the death rates of men outnumber that of women by almost three fold. These statistics have led to new and innovative research studies on oral and pharyngeal cancers and its probable link to HPV. If oral sex is a transmission route for HPV infection, then it would support these SEER findings. According to Sanchez-Vargas et al


<table>
<thead>
<tr>
<th>Anatomic Area</th>
<th>Average annual number of cases</th>
<th>HPV associated +</th>
<th>HPV 16/18 associated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>11,845</td>
<td>11,370</td>
<td>9,000</td>
</tr>
<tr>
<td>Vagina</td>
<td>714</td>
<td>714</td>
<td>400</td>
</tr>
<tr>
<td>Vulva</td>
<td>3,062</td>
<td>1,560</td>
<td>1,350</td>
</tr>
<tr>
<td>Anus &amp; Rectum</td>
<td>2,977</td>
<td>2,770</td>
<td>2,590</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>2,360</td>
<td>1,450</td>
<td>1,380</td>
</tr>
<tr>
<td>Total (Females)</td>
<td>20,903</td>
<td>17,610</td>
<td>14,720</td>
</tr>
<tr>
<td>Penis</td>
<td>1,000</td>
<td>360</td>
<td>310</td>
</tr>
<tr>
<td>Anus &amp; Rectum</td>
<td>1,618</td>
<td>1,500</td>
<td>1,410</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>8,936</td>
<td>5,630</td>
<td>5,360</td>
</tr>
<tr>
<td>Total (Males)</td>
<td>11,553</td>
<td>7,490</td>
<td>7,080</td>
</tr>
</tbody>
</table>

HPV-associated oral cancers have risen by 225% in young white men over the past 2 decades. If this trend continues, HPV-positive oropharyngeal cancers among white men in the United States will exceed cervical cancers among women by the year 2020. Obstetricians have the advantage of early detection of cervical cancer through the use of Pap smears which has greatly reduced the morbidity rate but it is important to note that women with a history of cervical cancer are 5-6 times more likely to develop oral cancer. With this statistic in mind, the dental professional can now see how important a thorough medical history can be and how an HPV positive response could impact an oral cancer screening.

In 2011, the American Dental Association “recognized HPV as a risk factor for oropharyngeal cancers but questions whether HPV is also responsible for other oral cavity cancers.” In a more recent press release, ADA said, “Because of the apparent increase in oropharyngeal cancer, and specifically cancers of the base of the tongue and the tonsils; these cancers associated with HPV, the release of ADA guidelines, and the heightened public awareness about HPV vaccines, dental health care personnel should be knowledgeable about HPV and its role in the development of oropharyngeal cancers.”

**Oral Cancer Screening Devices**

The medical field has been blessed with a multitude of early detection screenings for many cancers with annual prostate exams, mammograms and Pap smears to name a few. To date, dentistry does not have a universally accepted early detection device/screening/lab test for oral cancer according to the National Cancer Research Institute. We rely on visual and manual exams which are limited even if clinicians are doing them at every recare appoint-
ment. Oral cancer lesions may not be easily visible until the cancer has spread and become more invasive.

According to SEER and CDC reports, the survival rate of oral cancer from 2002-2008 was as follows:

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>Five Year Relative Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized (confined)</td>
<td>82.4</td>
</tr>
<tr>
<td>Regional (spread to regional lymph nodes)</td>
<td>57.3</td>
</tr>
<tr>
<td>Distant (metastasized)</td>
<td>34.9</td>
</tr>
</tbody>
</table>

Identifying any type of cancer at an early stage greatly increases the chance of survival but this chart helps remind us how important it is to identify oral cancer as early as possible.

There have been developments in the science of screening devices for oral cancer. These devices are not capable of detecting every cancerous lesion on every patient but they do help enhance visualization of the oral field with their physics-based technology of luminescence and fluorescence. These devices will not harm a patient, and if they can help detect oral cancer at an earlier stage, then its use and cost is justified.

Below is a list of tests used for HPV detection which are useful in answering epidemiologic or research based questions.

1. **PCR**: The most reliable test for the detection of HPV is with the polymerase chain reaction (PCR) test. It is used for a variety of purposes and aids in the detection and diagnosis of many infectious diseases. It is a biochemical technology that can amplify a single or a few copies of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence. The high sensitivity of PCR permits virus detection soon after infection, even prior to the onset of disease. Its products for identifying HPV-positive oral lesions as compared to cervical HPV-positive specimens are not as repeatable or reliable. The test only takes several hours and the basic steps are as follows:
   1. Obtain a sample
   2. Denature the DNA with a thermal cycler
   3. 2 separate strands of DNA now exist
   4. An enzyme called “Tag Polymerase” synthesizes the two strands of DNA
   5. The original DNA strand is duplicated so that each new strand contains one old and one new strand of DNA
   6. New strands can be duplicated 30-40 times

2. **Oral swabs or rinses**: As reported by Corstjens, Abrams and Malamud et al in JADA 2012, the use of these tests by dentists in the United States is moderate. Salivary tests can be done to detect a variety of viruses including HIV, HPV, Hepatitis C (HCV), Herpes simplex (HSV), Ebola or rabies. The tests are cost effective, easy to use and noninvasive. However, some targets for HPV detection are not in the saliva. This is why HPV nucleic acid-based tests detect the virus more accurately and are specific for oral HPV types. The nucleic acid test is usually a finger stick blood sample.

   Salivary testing became popular because saliva is rich in antibodies (IgA, IgM, IgG) and pathogens, particularly on the tongue and buccal mucosa. Most salivary diagnostic tests involve PCR where a sample is taken chairside and sent to a laboratory for analysis. Samples can be done three different ways:
   1. Oral Swab
   2. Expectorated saliva
   3. Expectorated oral rinse such as OraRisk® HPV test from Oral DNA Labs. This type of cultivation has the highest sensitivity because the sample is taken from the entire oral cavity.14 Swishing of the solution dislodges mucosal cells and the lab uses a variety of primers to detect as many HPV types as possible.

   Disadvantages of these tests can be the lack of standardization and the inability to identify the origin of HPV infection. They are also not the preferred method of diagnosis by medical professionals. Not all patients who have HPV-types in oral exfoliated cells are detected with HPV DNA in the primary tumor. According to the CDC, “these PCR tests are not useful clinically because their high analytic sensitivity detects...
low levels of HPV that is not predictive of disease requiring treatment.”

Advantages of these tests are they do permit the detection of persistent oral HPV infections for as long as five years after initial exposure and the cell yield and DNA-containing nucleated cells are more efficient than brush biopsy or scraping oral mucosa.16

3. Serum antibody tests.
This has been used as a marker of cumulative HPV exposure but its usefulness is limited.1 These tests cannot determine the exact site of mucosal exposure1,30 and not all persons exposed to HPV develop antibodies or antibodies may decrease over time as the immune system prevails over the virus. Again, most HPV infections are self-cleaning but some antibodies to the virus may remain. According to the CDC, “serological testing may be useful to monitor population exposure to HPV. As HPV infection is confined to the epithelium and infected cells are shed before cell death, natural HPV infection results in minimal host immune response and not all those infected have detectable antibodies. Serologic assays are currently available only in research settings.”

To date, there is no approved or recommended test for use in detecting high risk oral HPV types and there is no test presently on the market to predict the development of oropharyngeal cancer or oral disease associated with HPV infections.

Three tests are currently approved by the Food and Drug Administration (FDA) for detecting clinically significant levels of 13–14 high risk types of HPV when associated with cervical changes; however, none of these tests are approved for use in men, adolescents or detection of infected partners.

1. Digene HC2 High-Risk HPV DNA Test® by Qiagen, Gaithersburg, MD. Indicates the presence of one or more high risk types but does not indicate a specific type.
2. Cervista® HPV HR Test by Hologic, Bedford, MA. Indicates the presence of one or more high risk types but does not indicate a specific type.
3. Cobas® 4800 HPV Test by Roche Molecular Systems, Pleasanton, CA. Provides individual detection of HPV 16 and 18.

---

**HPV Vaccines**

Two vaccines are currently on the market in the United States with the intention of preventing the sexual transmission of many strains of HPV. Neither vaccine contains live virus but are composed of virus-like particles of the targeted HPV types. According to the CDC, 99% of study participants developed antibodies after receiving these vaccines. See Figure 15 for the CDC’s rates of vaccination in 2010.40

1. **Quadriivalent Vaccine: Gardasil®, Merck and Co, Inc.**
   This vaccine was approved in 2006 by the FDA for women and girls to protect against four HPV types including 2 low risk and 2 high risk HPV types; specifically the two low risk types; HPV 6 and 11 and the two high risk types; HPV 16 and 18. In 2009, the FDA amended the vaccine to include boys and men. The goal of this vaccine is to decrease the incidence of genital warts, and in cervical, anal, vaginal and vulvar cancers. The vaccine requires three doses for full protection.41

2. **Bivalent Vaccines: Cervarix®, GlaxoSmithKline**
   This vaccine was approved in 2009 by the FDA to protect against two high-risk types of HPV, types 16 and 18. Three doses are required for full vaccine protection.42

As with any vaccine, Gardasil® and Cervarix® are most effective if given prior to any HPV exposure. They do nothing for persons already infected with the virus. Due to the recent availability of these vaccines, it may be decades before Americans can see the true benefits of them. Reports of the effectiveness of protection range from 86-100%, however,
this is still truly unknown due to many factors such as the long latent period of some cancers, people not being aware when they have been exposed to HPV and the immaturity of the vaccines. In the years to come, we will see the true impact of these vaccines on human health.

**Conclusion**

There are many professionals presently researching HPV and its link to cancer. It is difficult for clinicians to practice evidence-based oral cancer screenings when many reports have contradictory results and inconsistent guidelines. In years to come, hopefully research will unravel the connection between HPV and the oral cavity so clinicians can provide appropriate preventive care for patients. Until then, we should all remember to take the time to do a thorough intraoral cancer screening. Five seconds of your time could change another’s life forever. It only takes 5 seconds to have a patient say “AHHH.” Not many healthcare professionals have regarding the anatomy of the oral cavity. We can have an enormous impact on the lives of those who get the opportunity to be in our chair.

**References**


Author Profile
Lisa Dowst-Mayo received her Bachelorette degree in dental hygiene from Baylor College of Dentistry in 2002. She has been active member in the tripartite of the America/Texas/Dallas & San Antonio dental hygiene associations since graduation and has held numerous leadership positions both at the state and local levels. She has worked as a full time clinical dental hygienist for the past 10 years and is currently employed at Dominion Dental Spa, the office of Dr. Tiffini Stratton, DDS. She is a published author and national lecturer; you can contact her through her website at lisamayordh.com.

Author Disclosure
Lisa Dowst-Mayo has no commercial ties with the sponsors or providers of the unrestricted educational grant for this course.
Questions

1. All of the following structures are visible intraorally EXCEPT the:
   a. Uvula
   b. Nasopharynx
   c. Palatine tonsils
   d. Esophagus

2. How many different strains of HPV have been positively identified through research?
   a. 50
   b. 90
   c. 120
   d. 200

3. Which of the following terms best describes a protein that has the potential to cause cancer through gene mutation, environmental influence or viral infection and is the target for cancer drug treatment?
   a. Oncogene
   b. Tumor-suppressor gene
   c. HPV
   d. None of the above

4. Which of the following is an oncogene?
   a. P53
   b. pRb
   c. E6
   d. HPV

5. Which of the following are inhibitors of tumor suppressor genes?
   a. E6
   b. p53
   c. E7
   d. Both a and c

6. Which of the following is a low risk HPV type?
   a. 11
   b. 16
   c. 18
   d. 33

7. Which of the following is a high risk HPV type?
   a. 16
   b. 42
   c. 43
   d. 44

8. HPV-4 can cause which of the following conditions in humans?
   a. Verruous carcinoma
   b. Squamous papilloma
   c. Verruca vulgaris
   d. Oral lichen planus

9. When oral lichen planus is linked to HPV, biopsy confirmed HPV type:
   a. 7
   b. 11
   c. 2
   d. 1

10. A lesion that appears as a papillary non-ulcerated gray-white or red mass with a broad base of attachment that commonly arises on the buccal mucosa or lip describes:
    a. Verruous carcinoma
    b. Verruca vulgaris
    c. Focal epithelial hyperplasia
    d. Condyloma acuminatum

11. Another name for venereal warts is:
    a. Verruous carcinoma
    b. Verruca vulgaris
    c. Focal epithelial hyperplasia
    d. Condyloma acuminatum

12. Venereal warts can be caused by HPV type:
    a. 2
    b. 16
    c. 18
    d. 7

13. Which condition is defined as a benign neoplasm with finger-like projections that resemble cauliflower and are related to HPV types 6 and 11?
    a. Squamous papilloma
    b. Verruous carcinoma
    c. Squamous cell carcinoma
    d. Focal epithelial hyperplasia

14. Heck’s disease is related to HPV types 13 and 32 and is also referred to as:
    a. Verruous carcinoma
    b. Verruca vulgaris
    c. Focal epithelial hyperplasia
    d. Condyloma acuminatum

15. The most commonly sexually transmitted infection in the United States is:
    a. HPV
    b. HIV
    c. Herpes
    d. Kaposis sarcoma

16. HPV can be transmitted by:
    a. Vaginal contact
    b. Oral sex
    c. Open-mouth kissing
    d. All of the above

17. When perinatal transmission of HPV occurs during childbirth, the greatest risk for the baby is:
    a. Genital warts
    b. Recurrent respiratory papillomatosis
    c. Heck’s disease
    d. There is no risk of transmission of HPV

18. The percentage of boys and girls who have engaged in oral sex by age 15 is:
    a. 20-25%
    b. 25-30%
    c. 50-60%
    d. 75-85%

19. The percentages of boys and girls who have engaged in oral sex by age 20 is:
    a. 20-25%
    b. 25-30%
    c. 50-60%
    d. 75-85%

20. HPV-positive oropharyngeal cancers are epidemiologically different from HPV-negative cancers. These cancers have an earlier onset and are associated with high-risk sexual behaviors.
    a. The first statement is true, the second statement is false
    b. The first statement is false, the second statement is true
    c. Both statements are true
    d. Both statements are false

21. 90-92% of head and neck cancers are diagnosed as:
    a. Squamous cell carcinomas
    b. Salivary gland tumors
    c. Sarcomas
    d. Lymphomas

22. Which of the following groups has the highest morbidity rates of oral and pharyngeal cancers?
    a. White men
    b. White women
    c. Black women
    d. Hispanic men

23. Which gender has a higher incidence of oral and pharyngeal cancers?
    a. Men
    b. Women
    c. Both men and women have the same rate of incidence
    d. Neither gender

24. Higher risk groups for HPV transmission include which of the following?
    a. Persons who have had over twenty six vaginal sex partners in their lifetime.
    b. Persons who have had more than six oral sex partners in their lifetime.
    c. Persons whose first sexual encounter was at a younger age
    d. All of the above

25. The five year relative survival rate for a person diagnosed with localized oral cancer is:
    a. 34.9%
    b. 57.3%
    c. 82.4%
    d. 100%

26. The five year relative survival rate for a person diagnosed with metastatic oral cancer is:
    a. 34.9%
    b. 57.3%
    c. 82.4%
    d. 100%

27. The technology used to test for HPV is:
    a. Culture and grows in a lab
    b. Molecular biological techniques
    c. Gram-stain technology
    d. Acid-fast staining of a culture

28. A biochemical technology test that can amplify a single or a few copies of a piece of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence is defined as which of the following?
    a. PCR testing
    b. Oral swab testing
    c. Serum antibody testing
    d. None of the above

29. Salivary tests can be performed to detect:
    a. HIV
    b. HPV
    c. Hepatitis C
    d. All of the above

30. Which of the following is correct regarding the effectiveness of HPV vaccines in preventing HPV?
    a. 25-35%
    b. 40-50%
    c. 50-75%
    d. 86-100%
It’s Time to Discuss Sex, HPV and Its Impact to Dentistry

Name: Title: Specialty:

Address: E-mail:

City: State: ZIP: Country:

Telephone (Home): Office ( ):

Lic. Renewal Date: AGD Member ID:

Requirements for successful completion of the course and to obtain dental continuing education credits: 1) Read the entire course. 2) Complete all information above. 3) Complete answer sheets in either pen or pencil. 4) Mark only one answer for each question. 5) A score of 70% on this test will earn you 3 CE credits. 6) Complete the Course Evaluation below. 7) Make check payable to PennWell Corp. For Questions Call 216.398.7822

Educational Objectives

1. Perform an intraoral cancer screening to ensure all aspects of the oral cavity are evaluated.
2. Describe HPV morphology, typing and virulence and their relevance to the identification of HPV related lesions.
3. Describe how HPV is transmitted and the related oral risks for patients.
4. Make well informed decisions before purchasing enhanced oral cancer and HPV screening devices, services etc.

Course Evaluation

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.

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. Please rate the usefulness and clinical applicability of this course.
   - 5 4 3 2 1 0

9. Please rate the usefulness of the supplemental webliography.
   - 5 4 3 2 1 0

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

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

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

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

14. How long did it take you to complete this course?

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

Please photocopy answer sheet for additional participants.

For IMMEDIATE results, go to www.ineedce.com to 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.)

If paying by credit card, please complete the following:

- Acct. Number: 
- Exp. Date: 

Charges on your statement will show up as PennWell

AGD Code 730

© 2014 by the Academy of Dental Therapeutics and Stomatology, a division of PennWell Corp.

Customer Service 216.398.7822

DMHPV1114DIG