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Oral HPV Infections and the Role of the Dental Professional

Oral Human Papilloma Virus Infections and the Role of the Dental Professional

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BACKGROUND

Human papilloma virus (HPV) is the most common sexually transmitted infection in the United States. More than 200 types of HPV have been identified with only a few of these having an oncogenic potential (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59). HPV has been associated with almost all cervical cancers, most anal cancers (~88%), and 70% of vaginal, 50% of penile, and 43% of vulvar cancers.[1] More recently, oral HPV infection (especially HPV 16) has emerged as one of the leading causes of head-and-neck cancers.

Oral HPV infection is present in 6.9% of the U.S. population and is more common among men.[2] HPV 16 (oncogenic type) is found in 1% of individuals. The prevalence of oral HPV is higher in men, smokers, immunosuppressed individuals, and those with a higher lifetime number of oral sex partners.[2,3] In normal conditions, oral HPV infections are not associated with malignant transformation, as they are cleared by the host within a year with an effective immune response against future HPV infections.[4-6] However, persistent infection may lead to both benign and malignant oral diseases.

HPV AND ORAL BENIGN LESIONS

Human papilloma virus–associated oral benign conditions include verruca vulgaris, squamous papilloma, condyloma acuminatum, and focal epithelial hyperplasia.

Oral Verruca Vulgaris

Oral verruca vulgaris (commonly called wart) presents as a pedunculated or sessile white nodule with a rough surface. (See Figure 1.) The hard palate, lips, and gingiva are the most common sites. It is associated with HPV 2, 4, and 57. Surgical excision is the treatment for oral verruca vulgaris.

Oral Squamous Papilloma

Squamous papilloma is a benign white or pink lesion with a cauliflower appearance associated with HPV 6 and 11 infections. (See Figure 2.) It usually affects the soft palate, tongue, lips, and gingiva. Scalpel excision is the preferred treatment.

Figure 1. Verruca vulgarism of the right palate

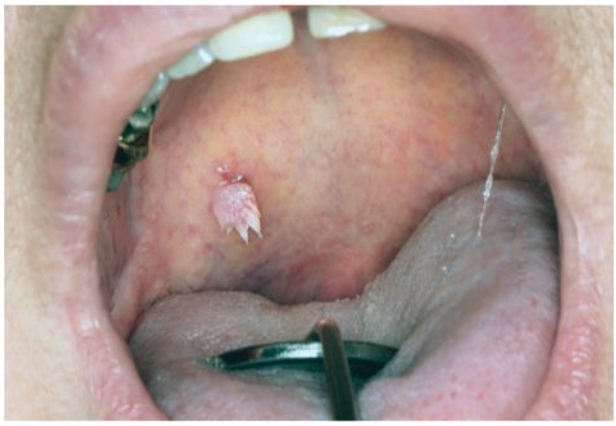

Figure 2. Squamous papilloma of the right posterior palate

Figure 3. Multiple condyloma acuminata of the lower labial mucosa in an HIV patient

Condyloma Acuminatum

Condyloma acuminatum is an HPV infection (mainly 6 and 11) predominantly of the anogenital mucosa. Oral condylomata, however, are sessile, pink, exophytic, papillary masses (usually >1 cm) typically seen in immunocompromised individuals or sexually active men. (See Figure 3.) They may affect the palate, labial mucosa, or lingual frenum. Treatment is with surgical excision.

Focal Epithelial Hyperplasia

Focal epithelial hyperplasia (FEH), or Heck's disease, is a rare HPV-associated condition (genotypes 13 and 32) associated with poverty, close living conditions, and dietary insufficiency. It is seen in children and adolescents of Inuit descent in Greenland and North Canada; indigenous people of North, Central, and South America; and descendants of Khoi-San in South Africa. FEH presents with multiple sessile, mucosal-colored papules, painless plaques and nodules of the tongue, labial, or buccal mucosa. Treatment includes surgery, cryotherapy, imiquimod, and interferon alpha.

HPV AND PREMALIGNANT CONDITIONS OF THE ORAL CAVITY

Recent studies have shown associations between HPV and leukoplakia, although they are uncommon and still controversial.[7-11] HPV-associated oral epithelial dysplasia is a unique histopathologic variant that presents clinically as white plaques, indistinguishable from non-HPV leukoplakia. The lesions mainly affect the lateral or ventral tongue and floor of the mouth. Treatment is excision with clear margins.[8]

HPV AND OROPHARYNGEAL CANCERS

Oropharyngeal cancer is the eighth most common cancer among males and the 13th most common among females in the United States, with a five-year relative survival rate of 66%.[12] An estimated 48,330 new cases of cancer of the oral cavity and pharynx are expected in the United States in 2016.[13] The main risk factors in the development of oral and oropharyngeal cancer are tobacco smoking, areca nut use, heavy alcohol consumption, and persistent HPV infection.[14,15] While the association between HPV and oral squamous cell carcinoma (SCC) is still unclear, oral HPV 16 infection causes the majority of oropharyngeal cancers in the United States. Oropharyngeal cancer is different from SCC and has incidence rates higher and rising more rapidly among men than women.[16] Chaturvedi et al. estimated that by 2020, the incidences of HPV-positive oropharyngeal cancers will be greater than the incidences of cervical cancer, and that by 2030, half of all head-and-neck cancers will be related to HPV.[17] Several methods and markers have been used to assess HPV infection in head-and-neck cancers, including HPV-DNA detection through PCR, HPV E6*I mRNA expression, and p16, pRb, p53, and Cyclin D1 protein detection. Castellsagué et al. have shown that HPV-positive oral and oropharyngeal cancer rates were 18.5% to 22.4% for the oropharynx and 3.0% to 4.4% for the oral cavity, when considering HPV-DNA plus E6*I mRNA and/or p16INK4a.[18]

The majority of head-and-neck HPV-related cancers are located in the oropharynx (mostly tonsils and base of the tongue).[16,18] The pathogenesis of HPV-related oropharyngeal cancer is mainly associated with the transforming activities of the E6 and E7 oncoproteins in high-risk HPV types. Patients with HPV-related oral cancer have a distinct demographic profile: they are, on average, younger, more commonly male, and have a higher socioeconomic status compared to HPV-unrelated oral cancer patients.[19,20] Patients with p16-positive oropharyngeal SCC (OPSCC) have favorable clinical outcomes compared to patients with p16-negative OPSCC.[21]

The signs of oropharyngeal cancer are not usually characterized by any visible oral lesion. Signs and symptoms include: a neck mass; persistent odynophagia; dysphagia; dysphonia; otalgia; a feeling of a lump in the throat; enlarged lymph nodes: or unexplained weight loss.[22] On the contrary, early signs of oral cancers are characterized by visible lesions in the mouth, including a persistent white and/or red lesion, a non-healing ulcer, progressive swelling, sudden tooth mobility without apparent cause, or an unusual oral bleeding or epistaxis.[23] If an oropharyngeal cancer is suspected, patients should be referred to a head-and-neck cancer specialist.[24]

DENTIST-PATIENT COMMUNICATION

Dental professionals have three main responsibilities related to HPV and risk reduction:

1. To educate themselves on the appearance of HPV-related signs and symptoms in order to perform more thorough examinations and oral cancer screenings
2. To educate patients on HPV and HPV-related cancers, including prevention, vaccination, self-screening instructions, and treatment
3. To encourage and refer patients to obtain HPV vaccination, particularly for boys and girls aged 11–12

Discussing both HPV infections and HPV vaccination can be a difficult topic to introduce to the dentist-patient relationship: dental professionals rarely discuss immunizations with their patients, and it is not a common topic when recording a comprehensive health history.[25] There are also concerns about the scope of practice and liability, raising the issue of sexually transmitted infections, time available during appointments, and lack of education on HPV in general.[26] Although some people might know that HPV vaccination can prevent cervical cancer, they might not be aware that the protection extends to HPV-related oropharyngeal cancers, as well, which makes the topic relevant to the dental setting. Dentists have a valuable opportunity to help prevent and treat HPV-related pathology for several reasons:

- Patients visit dentists more frequently than any other type of doctor, and tend to stay at one practice for longer periods of time. This allows for more conversation opportunities and a closer, trust-based relationship.
- Dentists and dental hygienists are already performing oral cancer screenings at each examination and making recommendations on reducing oral cancer risks.
- Dentists have a responsibility to be aware of patients' systemic health and should not feel reluctant to discuss oral-systemic connections, as many already do for conditions like diabetes, autoimmune diseases, and blood disorders.
- Many dental patients are unaware of the oral complications of HPV infection and might not know how to reduce their risk factors.[27]

Dentists and dental hygienists can be reassured that it is indeed within their scope of practice to discuss oral cancer risk reduction. The easiest way to begin is to introduce the topic in two instances: while taking a comprehensive health history and when performing routine oral cancer screenings. For the former, it is not necessary to mention sexual transmission at all, which can remove a significant barrier to comfortable patient communication. Whether recording a written or verbal medical history, a question inclusive of vaccination health as a whole can be a good way to begin: "Are you [or your children] current in all your immunizations, including HPV?" If patients are unfamiliar with current vaccination recommendations, dentists can easily mail or email the U.S. Centers for Disease Control and Prevention (CDC) immunization schedule (cdc.gov/vaccines). Since HPV is mentioned in particular, this opens the line of communication on discussing why a vaccination that may prevent oropharyngeal cancers is recommended by a patient's dental team.

During the oral cancer screening, dentists and dental hygienists can describe what they are looking for: "We'll be checking for any abnormal appearances or signs of possible pre-cancerous lesions or abnormal lymph nodes. Risk factors such as tobacco smoking and HPV can increase the possibility of oral cancer. Is this a good time to talk about reducing those risk factors?" Patients should pay attention during the oral cancer screening so that they can perform oral self-examinations at home. Grouping risk reduction, like smoking cessation, with a recommendation on HPV vaccination helps show patients that dentists are concerned with oral cancer prevention as a whole, which may reduce discomfort on raising an unfamiliar topic. Additionally, since one source of anxiety voiced by dentists is related to the limited amount of time available for appointments, this only adds minutes to parts of a dental examination that is already taking place. Particular attention should be paid to discussing HPV with parents so that children can be vaccinated during the ideal age window of 11–12 years old.

If patients are interested in vaccination (either for themselves or their children),

MASSACHUSETTS COALITION FOR HPV/CERVICAL CANCER & HPV-RELATED CANCERS AWARENESS DENTAL EDUCATION PROGRAM

According to the CDC, more than 20,000 women and approximately 12,000 men are diagnosed with HPV-associated cancers each year, with cervical cancer the majority in women and oropharyngeal cancer the majority in men.[28]

The HPV vaccine is recommended for both males and females 11–12 years old, as studies show it to be more effective prior to initiation of sexual activity. There has been much confusion surrounding the vaccine as a cancer prevention tool. Not surprisingly, HPV vaccination rates among young women thus far have been relatively low in comparison to other vaccines, and rates among young men are even lower. In addition, the vaccination protocol entails a series of three injections, adding complexity to the regimen and increasing the likelihood of essential doses to be missed. The vaccine has been shown to be highly effective in preventing HPV infection that may lead to cervical and other cancers.[29] Prophylactic vaccination is effective for the prevention of precancerous cervical and anal lesions, as well as for anogenital HPV infection in general. While there is still no definitive data on the effectiveness of the vaccination in the prevention of head-and-neck cancers, studies have shown that HPV vaccination may reduce the incidence of this malignancy.[30] Therefore, it is imperative to increase vaccination rates among youth in the United States. In addition, recent research supports that "vaccination efforts should be focused on low-income and minority women, who have the greatest burden of disease."[31] Dedicated, trained dental professionals may be underutilized assets in the realm of HPV education and oral cancer prevention.

The Massachusetts Oral HPV/Prevention Taskforce's purpose is to educate dental professionals about the connection between HPV and oral, cervical, and other cancers. Dental professionals are introduced to tools for talking to patients about the HPV vaccine as cancer prevention. Primary responsibilities of this program are to educate dental offices and dental professionals on HPV and the HPV vaccination. Related items include:

- Educational materials/tool kits for dental offices, which include brochures, prescription referral pads, posters, and a "Tips for Talking" information sheet for dentists
- An HPV education program at the Yankee Dental Congress dental conference in Boston in January 2017
- Educational presentations in dental offices in the New England region
- Development of a subcommittee group under the HPV/Cervical Cancer Work Group
- Partnership with the Massachusetts Dental Society

dentists can supply information and referrals. Patients should be told that HPV vaccination is normally covered for all genders between the ages of 9 and 26 and is most effective when given by age 13, which is when the immune system has an ideal response. Dentists can give patients referral forms that recommend HPV vaccination and follow up to ask when the injection series has been completed. Patients can also be given information on local vaccination clinics, including hours, locations, and phone numbers of retail pharmacies and local health clinics, if they don't already have a primary care physician.

Dentists have multiple opportunities to make a significant impact in educating patients about HPV, HPV-related pathology, and prevention. Dental professionals should become familiar with and educated on the topic themselves so they can provide information and be proactive in reducing HPV lesions, risk factors, and oral cancers. **JMDS**

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