Oral HPV – Oropharyngeal Cancer, Prevention, and Patient Communication

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HPV: What is it?

- **Human Papilloma Virus**
- Spread by skin-to-skin contact
- Can infect the genital and oral/pharyngeal skin of all genders at all ages
HPV Types Differ in their Disease Associations

~40 Types

- Mucosal sites of infection
  - High risk (oncogenic)
    - HPV 16, 18 most common
  - Low risk (non-oncogenic)
    - HPV 6, 11 most common
  - Cervical Cancer
  - Anogenital Cancers
  - Oropharyngeal Cancer
  - Cancer Precursors
  - Low Grade Cervical Disease

~80 Types

- Cutaneous sites of infection
  - "Common" Hand and Foot Warts
  - Genital Warts
  - Laryngeal Papillomas
  - Low Grade Cervical Disease

~5 Types
Every year in the United States 27,000 people are diagnosed with a cancer caused by HPV. That's 1 case every 20 minutes.
How common is HPV?

• HPV is the most common STI in the US today; 80% of people who are sexually active will have HPV at some point.

CDC image
HPV is found in those who have not had vaginal sex

Study on women who have not had PIV (penis-in-vagina) sex

- HPV was found in 46% of the women; almost half of the women had HPV before ever having sex
- 70% of these women reported non-coital (no vaginal sex) sexual behaviors that may in part explain how they got HPV; intimate contact can spread HPV
- Oral sex can lead to oral HPV infection

Shew, J Infect Dis. 2012
How is HPV spread?

- Any type of intimate sexual contact, genital touching or rubbing
- Penetrative intercourse is **NOT** necessary to get HPV
- Most commonly spread through sexual intercourse (genital-genital, anal-genital, oral-genital, manual-genital)
- Condoms do not always prevent transmission

How do you know if you have HPV?

- Most people with HPV don’t have any symptoms
- Oral and genital warts – Non-oncogenic
- Pre-cancerous lesions and leukoplakia
  - HPV can be detected in biopsy
- Most infections cannot be detected
- Most infections are cleared by the body
Is there treatment for HPV infection?

- There is currently no treatment for HPV infections.
- HPV is a virus, so it cannot be cured with antibiotics.
- Some genital lesions and warts that can result from HPV infections can be treated.
- Like all viruses, HPV can live in the body for many years. The infection can remain inactive for decades, then reactivate later in life as the immune system weakens.
How does HPV cause cancer?

How does HPV cause cancer?

- HPV infects basal keratinocytes in skin and mucus membranes
- Estimated that 43-62% of genital swabs would harbor HPV
- Many people will clear infection
- Expression of L1 and L2 capsids lead to viral proliferation but not carcinogenesis
- HPV DNA incorporation leads to expression of E6 and E7 oncogenetic proteins → necessary for carcinogenesis

<table>
<thead>
<tr>
<th></th>
<th>Percent change</th>
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<tbody>
<tr>
<td>Overall</td>
<td>62.6</td>
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<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>81.8</td>
</tr>
<tr>
<td>Female</td>
<td>-1.6</td>
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<tr>
<td>Race</td>
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<tr>
<td>White</td>
<td>87.7</td>
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<tr>
<td>Black</td>
<td>-18.3</td>
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<tr>
<td>Other</td>
<td>5.9</td>
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<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>68.5</td>
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<tr>
<td>40-49</td>
<td>73.1</td>
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<tr>
<td>50-59</td>
<td>81.2</td>
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<tr>
<td>60+</td>
<td>51.3</td>
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</table>

Surveillance, Epidemiology, and End Results (SEER) – NIH – National Cancer Institute
HPV-related cancers are growing rapidly

The rate of new head and neck cancers increased in the past 20 years

During this time:
• Smoking and alcohol-related head and neck cancers decreased 50%
• HPV-related head and neck cancers increased by 225%
Why such a significant increase?

- Not necessarily increase in HPV infections (HPV-negative OPC also on the rise)
- Possible connections to decreasing tobacco consumption
- Significant increase in older men
- Co-morbidities with alcohol, tobacco, poor nutrition, increased number of sexual partners

- **Focus on prevention with vaccination and awareness of signs and symptoms**

Schache et al. *Cancer Research* November 2016 76 [22]
Oropharyngeal Cancer

Risk Factors:

• HPV 16 and 18

• 49,670 new cases are expected in the United States in 2017

• > 70%: HPV infection

Scully C et al., 2009
D'Souza et al., 2007
Testing Positive for HPV 16 and 18

- Positive HPV 16 and 18 are important risk factors for OPC

- However, frequent testing and biopsies may involve increased expense, morbidity from diagnostic procedures, and significant anxiety

- Much of the general population has HPV

- Important to be aware of high-risk symptoms

Symptoms to Prompt Referrals

- Dysphagia
- Feeling of “fullness” in throat
- Neck swelling
- Lymphadenopathy
- Limited tongue movement
- Hemoptysis
- Unilateral sore throat
- Unilateral enlarged tonsil
HPV Prophylactic Vaccines

- Recombinant L1 capsid proteins that form “virus-like” particles (VLP)
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection
## HPV Vaccines Currently Licensed in U.S.

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Bivalent 2vHPV (Cervarix)</th>
<th>Quadrivalent 4vHPV (Gardasil)</th>
<th>9-Valent 9vHPV (Gardasil 9)</th>
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</thead>
<tbody>
<tr>
<td>GlaxoSmithKline</td>
<td>Hypersensitivity to latex*</td>
<td>Hypersensitivity to yeast</td>
<td>Hypersensitivity to yeast</td>
</tr>
<tr>
<td>HPV Types Included</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Dose Schedule</td>
<td>3 dose series: 0, 1, 6 months</td>
<td>3 dose series: 0, 2, 6 months</td>
<td>3 dose series: 0, 2, 6 months</td>
</tr>
</tbody>
</table>

* May be present in tip of pre-filled syringes
Updated Dosing

• Up to age 15 – Only two injections needed
• Ideal age window: 11-12 (pre-exposure and ideal immune response)
• Widened gap between doses? Finish series
• Age range covered by most insurance: 9-26
• Retail pharmacies: Now starting at age 9
• Immunizations for adults over 26?
Is the vaccine safe & effective?  
Are there side effects?

- The vaccine is safe and very effective
- More than 60 million doses of HPV vaccine given in US since 2006
- Over 170 million doses worldwide (Europe, Australia)
- Side effects are mild; redness, soreness at injection site, mild fever, and upset stomach (similar to the ones with all vaccines like meningitis and tdap)
- No serious side effects found to be caused by vaccine
Vaccine Efficacy

• Rates of HPV infection targeted by vaccine fell from 11.5% in 2003-2006 to 5.1% in 2007-2010

• Effectiveness of getting at least one shot was 82%

• From the 79 million doses of Gardasil distributed since 2006, <0.1% have had a reported serious adverse event

• More than 175 million doses of HPV vaccine have been distributed worldwide and 57 million doses have been distributed in the United States. In the seven years of HPV vaccine safety studies and monitoring that have been conducted since the vaccine was licensed, no serious safety concerns have been identified. *Reports to the Vaccine Adverse Event Reporting System (VAERS) have decreased each year since 2008.*

Markowitz, et al, J Infectious Dis, 2013
Efficacy

• Review of 20 studies in 9 countries
• In countries with >50% coverage, among 13-19 year olds
  – HPV 16/18 prevalence decreased at least 68%
  – Anogenital warts decreased by ~61%
• Evidence of herd effects

Drolet et al. Lancet Infect Dis 2015
Australian study of 39,000 girls found vaccination by age 14 is twice as effective at preventing abnormal cell changes

The study looked at girls who were vaccinated between age 14 and 17:

• It showed a 75% reduction in cervical pre-cancer for girls vaccinated by age 14
• It showed a 35% reduction in cervical pre-cancer for girls vaccinated after 14
• The vaccine was twice as effective in 14 year olds because they had a better immune response and were less likely to have been exposed to HPV
Concerns About Vaccine Safety

A wealth of data has found **no increase** in incidences of:

- **2011** - allergic reactions, anaphylaxis, Guillain–Barré Syndrome, stroke, blood clots, appendicitis, or seizures
  (compared to people who were unvaccinated or who received other vaccines)
- **2013** – (almost 1 million girls) blood clots or AEs related to the immune & CNS
- **2014** – (>1 million women) venous thromboembolism or blood clots
- **2012 and 2014** – (2 studies) autoimmune disorders
- **2015** – Multiple sclerosis or other demyelinating diseases
- **2015-** POTS or CRPS (European Medical Review)
- **2012** – Vaccine may be associated with skin infections around injection site and fainting on administration, to similar levels with other vaccines

Key Findings – CDC and Non-CDC

• Venous thromboembolism (VTE)
  – Study evaluating the risk of VTE in vaccinated persons age 9-26 years
  – *Found no increased risk of VTE following 4vHPV*

• Autoimmune and neurologic conditions
  – Study addressing concerns about autoimmune and neurologic disease following 4vHPV vaccination.
  – *Found no association between 4vHPV vaccination and 16 autoimmune conditions*

• Injection site reactions and syncope
  – 4vHPV vaccination may be associated with skin infections where the shot is given during the two weeks after vaccination and fainting on the day the shot is received
  – *No major safety concerns found*

1. Gee et al., Vaccine 2011
Vaccination does not change sexual behavior

Three large studies including more than 200,000 girls and young women found that HPV vaccination is NOT associated with:

- Being sexually active
- Having an increased number of sexual partners
- Receiving counseling on contraceptives
- Testing for or diagnoses of sexually transmitted infections

Bednarczyk RA, *Pediatrics* 2012;130:798
Patient Communication About HPV:
The Role of the Dental Professional
Why dental professionals?

We can make a significant difference.

• Educating on HPV
• Explaining that HPV causes oral cancers
• Showing how to perform oral cancer screenings
• Referring patients to get vaccinated
Valuable Opportunity

- At least two exams per year
- Long-term patient relationship
- Treating children and their parents
- Community involvement
Initial Reluctance From Dental Professionals

- Immunizations not normally discussed in health history
- Limited knowledge on the topic
- Discomfort with discussing STIs
- Insufficient time during appointments
- Scope of practice concerns

Raising the Topic

• Medical history form – Include immunizations

• Verbal medical histories are the best way.
  – More thorough
  – Extrapolation on any “yes” answers
  – Begin the provider-patient relationship
  – Clues about personality, medical literacy
  – Source of referrals: Back to PCP, addiction and cessation resources, systemic health concerns
List of medications, drugs, and supplements:

Birth Control?

Allergies (drugs, food, materials)

Do you currently or have you ever had any of the following problems (Click only if "Yes")

☐ Artificial heart valve or joints, congenital heart defects, history of endocarditis
☐ Gastrointestinal disorders
☐ Heart attack, stroke, cardiac issues
☐ Psychiatric or emotional diagnoses
☐ Ever taken any medication (besides those listed above) for longer than 1 month?
☐ Any history of addiction, including eating disorders?
☐ High blood pressure
☐ Congenital, genetic, or autoimmune conditions
☐ Mobility or sensory impairment
☐ Don't feel safe at home
☐ Diabetes, endocrine disorders, thyroid disorders
☐ HIV/AIDS
☐ Cancer, radiation, chemotherapy
☐ Current on immunizations, including HPV?

Detail for any "Yes" responses or anything not covered

Caries, Nutrition, and Food Security Questions

☐ Do you add sugar to your tea or coffee?
☐ Do you have daily sweets or sugary drinks?
☐ Do you or your family need resources to help in purchasing food or groceries?
Pediatric Medical History

Patient:

List of medications, vitamins and supplements:

List of surgeries, major illnesses, and emergency room and/or hospital visits:

Current on immunizations including HPV if over age 9?

Allergies to drugs, food, or materials:

Behavioral notes, including dental anxiety or questions:

Pediatrician name and clinic:
Medical History

• Include a question on immunizations in general:
  – “Are you (or your child) current on all immunizations, including HPV?”
  – “Would you like a link to or printout of the current CDC immunization schedule?”
  – www.cdc.gov/vaccines
Explaining HPV

What to say:

• HPV is a virus that can cause cancers in several parts of the body, including the mouth and throat.

• We’ll be doing an oral cancer screening today and will teach you how to do self-screenings at home.
Explaining HPV Vaccine

What to say:

- There is a vaccine that protects against this cancer-causing virus. It works *really* well and is the only vaccine that prevents cancer!
- To be most effective, your child should be vaccinated by age 13
- The vaccine is very safe
- Most insurances cover the vaccine from ages 9-26
Explaining HPV Vaccination

What to say:

• Your child is now eligible for HPV vaccination, and I’ll refer him or her to their pediatrician to start the immunization process.

• While you’re there, please check in on their other vaccinations, like TDAP. (“Same day, same way”)

• Adults can also benefit from HPV vaccination.
Addressing Patient Concerns

• Remember that people who don’t arrive at conclusions from data might not respond well to data. (Don’t be condescending)

• General reassurance that you would get it for yourself, your patients, and your children

• Many blogs and anecdotes of general “not doing well at school” – source of unsupported fears of vaccines – Separate from “traditional” antivaccination concerns

• Use the same types of arguments you find effective when discussing fluoride, mercury amalgam, and radiography
Important to Discuss Transmission?

• If that is your main barrier, drop it and focus on cancer screening and encouraging vaccination.

• Almost everyone has HPV anyway, and it is easily transmitted by skin contact

• Encouraging vaccinations for ages 9-12 (rather than older teenagers) might help separate it from a discussion about STIs.

• Remind parents and patients that all genders should be vaccinated and screened.

• All of these patient discussions can occur without mentioning the phrase “STI”.
Explaining HPV Vaccine

• Remind patients that it is given in either 2 or 3 doses.

• Give patients referrals to go to their PCP, health clinic, pharmacist, or other immunization provider.

• Encourage parents and patients to keep you updated with their injection dates.
The CHC Opportunity

- Comprehensive medical home
- Follow-up on referrals
- Gather data on vaccine rates
- Dentists can help educate physicians and pharmacists
Reasons parents won’t initiate HPV vaccination for children

- Not recommended
- Safety concern/Side effects
- Not needed or necessary
- Lack of knowledge

MMWR 2014; 63(29);625-633;
The Oral Cancer Screening

• Tell your patients you’re doing one!
• Many patients are unaware that HPV causes OPC and how to reduce their cancer risk factors.
• Have them watch screening in the mirror so they can perform self-screenings.
• Educate yourselves and patients on lymphadenopathy and palpation.

HPV-related cancers can be different!

- HPV primarily causes oropharyngeal cancer
- Different from squamous cell carcinoma (SCC) of the mouth
- Some support that HPV can either cause SCC or make it more difficult to treat
- Screening for oropharyngeal cancer is mainly by asking patients questions about their symptoms

HPV Dysplasia – SCC connection

An example out of 20 cases:

- 17 men, 3 women
- Median age 56 years
- 13 lateral/ventral tongue
- All had the exact same unusual dysplasia
- All were high risk HPV positive, p16 positive
- 2/10 developed HPV-positive SCC
Examining the oral cavity

Photographs courtesy of Dr. Allessandro Villa
Oral cancer
HPV+ leukoplakia with dysplasia – Not cancer
HPV+ squamous cell carcinoma
Oropharyngeal cancer signs/symptoms

- A sore throat that does not go away
- Trouble swallowing
- Trouble opening the mouth fully
- Trouble moving the tongue
- Ear pain
- A lump in the back of the mouth, throat, or neck
- A change in voice
- Coughing up blood
- Enlarged lymph nodes or weight loss

ADA and NCI
Patient questions

• “Have you had any difficulty swallowing, a sore throat on one side for a long time, or enlarged lymph nodes?”

• Differentiate from respiratory virus

• Ask while leaning the chair back – No extra time needed

• Encourage monthly self-exams, “Along with your monthly breast self-exams”, which patients are already familiar with

ADA, statement and NCI
Massachusetts HPV Oral Prevention Task Force

• Representatives from local hospitals, cancer treatment centers, public health government, private practice, and nonprofits
• Toolkits
• My contact: drwagner@smilesbyrosie.com
• Introducing Kelly Welch
HPV Education & Toolkits Program: Major Contributions from

Academy of General Dentistry
Commonwealth of Massachusetts Department of Public Health
American Cancer Society
American Academy of Pediatrics
National Network of Libraries of Medicine
BWH Brigham and Women’s Hospital
SMILES by Rosie
Toolkits Designed by

Oral HPV Taskforce
Understanding of the connection between HPV and cancer
Understanding of the role the HPV vaccine plays in cancer prevention
Comfort in discussing HPV and the HPV vaccine with patients
Dentist’s commitment to cancer screenings
Components of Toolkit

Script Pad

Talking Tips Sheet

Tips for Talking about HPV at the Dentist

Although dentists and hygienists know the importance of oral cancer screenings and the role HPV vaccination plays in cancer prevention, it can be difficult to know how to talk about it.

HOW DO I START THE CONVERSATION?

“Did you know that your pediatrician recommends a vaccine that can prevent HPV, and that HPV can cause cancer? Your child is the right age to be vaccinated. It's time to ask your pediatrician about it.”

PARENTS MAY ASK...

What is HPV?

YOUR ANSWER...

HPV (human papillomavirus) is the most common sexually transmitted infection in the USA. It can cause genital warts and many types of cancer, including oropharyngeal and cervical.

PARENTS MAY ASK...

How common is HPV and HPV-related cancer?

YOUR ANSWER...

Nearly everyone will have HPV in their lifetime, usually with no symptoms or treatment needed. But HPV does cause 31,000 cancer cases each year in the USA, about 11,000 of which are oropharyngeal cancers.

PARENTS MAY ASK...

Why is it important now?

YOUR ANSWER...

If administered before age 15, the immune response is so strong that boys and girls only need a 2 shot series. After age 15, they need 3.
Components of Toolkit

Brochure for Patients

Understanding HPV & Cancer at the dentist

Office Poster

CANCER PREVENTION for your child starts at the DENTIST!

HPV and the Cancer Connection

HPV (Human Papillomavirus) is spread by intimate skin-to-skin contact.

Nearly 79 million people in the USA are infected, often without knowing it.

Some types of HPV can infect parts of your body and cause cancer of the tongue, tonsils, throat, cervix, vulva, vagina, anus, and penis.

Almost 22,000 people a year will develop HPV-related cancer in the USA, and 4300 people will die.

Doctors recommend that boys & girls age 11-12 receive the HPV vaccine to prevent cancer. Talk to your pediatrician about getting the HPV vaccine.
Where to access resources

www. TeamMaureen.org

– FREE DOWNLOAD of Toolkit in English, Spanish, and Russian
– Additional resources on HPV infection and HPV-related cancer
– Contact me at Kelly@TeamMaureen.org
– Join the MA Coalition to stay connected to HPV-related cancer news
Thank you!