Human Papilloma Virus: A Quick Taste of Cancer Prevention from an Oral Health Perspective

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2015 NH Oral Health Forum
Concord, New Hampshire
October 30, 2015
Objectives

• **H**one our understanding of the role of HPV and its links to oral cancer.

• **P**revent the spread of HPV infections and cancers.

• **V**erbalize why HPV surveillance and prevention are important.
What makes HPV such a hot topic?

ADA Council on Scientific Affairs:
Statement on Human Papillomavirus and Squamous Cell Carcinomas of the Oropharynx

“The rising incidence of oropharyngeal cancer (specifically oropharyngeal squamous cell carcinoma) associated with HPV is a significant concern for the health care community.”
What makes HPV such a hot topic?

- Over the past 25 years
  - HPV infection has become firmly established as an etiologic risk factor for **cancers of the oropharynx**
    - Specifically of the tonsils & base of the tongue
  - Recent study:
    - 225% increase in HPV-positive oropharyngeal cancers during 1988 to 2004
    - 50% decrease of HPV negative cancers over the same period

What makes HPV such a hot topic?

• According to the ADA Council on Scientific Affairs:

  “Dental care providers are encouraged to educate themselves and their patients about the relationship between HPV and oropharyngeal cancer, especially the growing prevalence of these cancers in younger non-smokers and non-drinkers. . .”
More Questions than Answers for the Medical and Dental Communities?

- Does kissing transfer Human Papilloma Virus making other people susceptible to oral cancer?
  - How much of a deep passionate kiss do you need to transfer HPV?
  - How would you even begin to test this assumption?
- Is a child at risk if the mother is positive?
- Can HPV be transferred if a mother tastes her baby’s food before giving it to her child?
- Is an HPV positive person more at risk if using tobacco & alcohol together?
  - Is one more of a risk than the other?
  - Is a person who is genetically susceptible to cancer more affected by this trio?
- Is HPV an entity that can be harbored for years and then reappear?
  - Do you recheck positive patients again and at what intervals?
  - Do you check entire families for HPV, and if so how often?

Burkhart, Nancy W.  RDH (Registered Dental Hygienist). HPV: To test or not to test. (http://www.rdhmag.com/articles/print/volume-30/issue-12/features/hpv-to-test-or-not-to-test.html)
More Questions than Answers for the Medical and Dental Communities?

• Do you test all patients for HPV, or just some high-risk groups?
  – Do you check adolescents who may or may not admit to sexual activity?
  – Do you talk to the parent first without even asking? What would be the reaction of parents?
  – Adolescents and even much older adults do not consider oral sex to be “true” sex, so how crucial is phrasing and communication?

• Who should talk with patients about the illness or test results?
  – How confidential is the information?

• Do you test patients for HPV who have had previous oral cancer at every appointment?
  – What is the accuracy of testing?

• Does the constant bleaching of teeth affect the oral tissues in some individuals? (as practiced by many under the age of 40)
  – Does HPV affect this tissue before or after bleaching?

• Does gastro esophageal reflux disease and frequent heartburn make oropharyngeal tissues more susceptible to HPV in some individuals
  – Possibly those with a genetic predisposition?

Burkhart, Nancy W. RDH (Registered Dental Hygienist). HPV: To test or not to test. (http://www.rdhmag.com/articles/print/volume-30/issue-12/features/hpv-to-test-or-not-to-test.html)
More Questions than Answers for the Medical and Dental Communities?

• With regard to HPV
  – Are you now being asked to counsel patients about sexual practices and personal medical information?
  – If you do provide this counseling, what are the long-term ramifications?
What is Human Papilloma Virus (HPV)?

• HPV is a very common virus that spreads between people when they have sexual contact with another person.
• HPV infection can cause cervical cancer in women (and penile cancer in men).
• HPV causes anal, oropharyngeal and throat cancers, and genital warts in both men and women.
Human Papilloma Virus

• Most common sexually transmitted viral infection in the US
• There are nearly 200 different strains of HPV
  – Most are harmless and not cancer causing
  – 9 are known to cause cancers
  – HPV 16 most likely to cause oral cancers
    • also associated with cervical, anal, and penile cancers
  – Additional 6 suspected of causing cancers
• You can have HPV without ever knowing it
  – No obvious signs or symptoms
  – Body often clears it before detection

http://www.oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php#sthash.QcCCL0uf.dpuf
Oropharyngeal Squamous Cell Carcinoma

- 95% of laryngeal cancer
- ~11,000 new cases diagnosed in US annually
- Risk Factors
  - Chronic HPV (RR~230)
  - Tobacco & alcohol (RR>100)
  - Tobacco abuse (RR~14-35)
  - Excess ETOH use (RR~16)
  - Infrequent F/V (RR~2.7)

www.slideshare.net%2Fdoctorbobm%2Fviruses-and-cancer

Courtesy of Dr. David C Fredenburg
Average Number of Newly Diagnosed HPV-Associated Cancers by Sex, in the United States (2005-2009)

Women (N=20,413)
- Cervix: 55% (n=11,279)
- Vulva: 15% (n=3,039)
- Oropharynx: 11% (n=2,137)
- Anus: 15% (n=3,084)
- Vagina: 4% (n=694)

Men (N=12,002)
- Oropharynx: 78% (n=9,312)
- Penis: 8% (n=1,003)
- Anus: 14% (n=1,687)


www.cdc.gov/vaccines/youarethekey
Oral Cancer Signs and Symptoms

- Oral ulcer/sore without healing over 2-3 weeks
- Difficult or painful swallowing
- Pain when chewing
- Persistent sore throat or hoarse voice
- Swelling or lump in the mouth
- Persistent painless lump in the neck
- Numb feeling in the mouth or lips
- Constant coughing
- Persisting one-sided earache

http://www.oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php#sthash.QcCCL0uf.dpuf
Human Papilloma Virus

• Leading cause of oropharyngeal cancers
  • HPV 16 is most responsible
  • Affects both males and females
  • Accounts for a very small number of front of the mouth, oral cavity cancers
  • Found primarily posteriorly
    • base of the tongue
    • back of the throat
    • tonsils
    • tonsillar crypts/pillars

http://www.oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php#sthash.QcCCL0uf.dpuf
How do people get oral HPV?

- Few studies have looked at how people get oral HPV
- Some show conflicting results
- Oral HPV may be passed during oral sex
  - Mouth-to-genital or mouth-to-anus contact
  - Open-mouthed ("French") kissing
  - Likelihood of getting HPV from kissing or having oral sex with someone who has HPV is unknown
  - Long time sexual partners probably tend to share genital HPV
- More research is needed to understand exactly how people get/give oral HPV infections

www.cdc.gov/std/hpv/stdfact-hpvandoralcancer.htm
Human Papilloma Virus Testing

- Oral HPV testing in both men and women is problematic
  - Commercial tests available in the dental community
    - of unclear value
    - positive testing does not prove persistence of the infection
  - There are no visible oral signs of initial HPV infection
  - There are also no well established genital tests for men
- For women:
  - Routine HPV/Pap testing recommended during cervical exams

http://www.oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php#sthash.QcCCL0uf.dpuf
Human Papilloma Virus

• Most people clear the virus naturally
  – Never knowing they were exposed or had it
• If test positive for HPV
  – No sure way to know when they were infected with HPV
  – Who gave it to them
  – Does not mean that someone is having sex outside of their current relationship
  – With higher risk/cancer causing strains, cancer may not develop
• HPV is believed to have long periods of dormancy
  – Causing negative test results
  – Before it is detected or develops into a cancer

http://www.oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php#sthash.QcCCL0uf.dpuf
HPV Infection

• Most American females and males will be infected at some point in their lives with at least one type
  – Current estimate is 79 million
  – 14 million new infections yearly
  – Most common in teens and early 20’s

• Most people will never know they have been infected

HPV Transmission

• HPV exposure can occur with any type of intimate sexual contact
• Intercourse is not necessary to become infected
• Nearly 50% of high school students have already engaged in sexual (vaginal-penile) intercourse
  – 1/3 of 9th graders and 2/3 of 12th graders have engaged in sexual intercourse
  – 24% of high school seniors have had sexual intercourse with 4 or more partners

HPV is found in virgins too!

- Study of adolescent women without prior vaginal intercourse examined the frequency of vaginal HPV and the association with non-coital sexual behavior
  - HPV was detected in 46% of women prior to first vaginal sex
  - 70% of these women reported non-coital behaviors that may in part explain genital transmission

HPV & Cervical Cancer

• Cervical cancer is the most common HPV-associated cancer among women
  – 500,000+ new cases and 275,000 attributable deaths world-wide (2008)
  – 12,000+ new cases and 4,000 attributable deaths in the U.S. (2011)
  – 25.9% cervical cancers occur in women who are between the ages of 35 and 44
    – 14% between 20 and 34
    – 23.9% between 45 and 54
HPV-Associated Oropharyngeal Cancers

- Prevalence increased from 16.3% (1984-89) to 71.7% (2000-04)
- Population-level incidence of HPV-positive cancers increased by 225%!
  - while HPV-negative cancers declined by 50%
- More oropharyngeal cancers that were previously thought to be caused by tobacco and/or alcohol use are now identified as HPV-related cancers

www.cdc.gov/vaccines/youarethekey
### Economic Impact Related to HPV-Associated Disease, 2010

<table>
<thead>
<tr>
<th>Event</th>
<th>Cost ($ billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cancer screening*</td>
<td>6.6</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>0.4</td>
</tr>
<tr>
<td>Other anogenital cancers</td>
<td>0.2</td>
</tr>
<tr>
<td>Oropharyngeal cancer</td>
<td>0.3</td>
</tr>
<tr>
<td>Anogenital warts</td>
<td>0.3</td>
</tr>
<tr>
<td>RRP**</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>8.0</strong></td>
</tr>
</tbody>
</table>

* Cervical cancer screening costs: ~ 80% routine screening, ~20% follow-up

** RRP costs: ~ 70% juvenile-onset, ~ 30% adult-onset


RRP: recurrent respiratory papillomatosis

Reprinted with permission from: www.cdc.gov/vaccines/youarethekey
What are the numbers?

- There are currently 26 million girls <13 yo
- If none of these girls are vaccinated then:
  - 168,400 will develop cervical cancer
  - 54,100 will die from it

- Vaccinating 30%:
  - would prevent 45,500 of these cases and 14,600 deaths

- Vaccinating 80%:
  - would prevent 98,800 cases and 31,700 deaths

www.cdc.gov/vaccines/youarethekey
What are the numbers?

For each year we stay at 30% coverage instead of achieving 80%, there will be an additional:

- 4,400 future cervical cancer cases
- 1,400 cervical cancer deaths nationally
What are the numbers locally?

- Attention is being focused on the continued low rates of HPV vaccination throughout the country.
- By extrapolation, **New Hampshire** will have:
  - 19 cervical cancer cases per year
  - 6 cervical cancer deaths per year
- New Hampshire is NO exception:
  - Currently, only 34.5% of females 13 to 17 years of age have completed the 3 series dose.
Complications of HPV Infection

If trends continue, the annual number of HPV-positive oropharyngeal cancers is expected to surpass the annual number of cervical cancers by the year 2020.

This is no longer just a women’s healthcare issue!
Human Papilloma Virus

• The fastest growing segment of the oropharyngeal cancer population:
  • Otherwise healthy
  • non-smokers in the 25-50 age range
• Most at risk population:
  • White, smoking/drinking males, ages 30 to 64
    • ~2.5x more likely than females
  • Increased #’s of sexual partners

http://jama.jamanetwork.com/article.aspx?articleid=1104983&resultClick=3
Oral HPV Numbers

- Estimated = 2.1+ million infected in the US
- Prevalence = 7% of population (14 to 69 yo)
  
  ♂ > ♀

- HPV 16 incidence = 1% of population (14-69 yo)
- 90% of HPV positive Oral Squamous Cell Carcinomas linked to HPV type 16

http://jama.jamanetwork.com/article.aspx?articleid=1104983&resultClick=3
“Persistent HPV infection can cause cancers of the cervix, vagina and vulva in women, cancer of the penis in men, and cancers of the anus and the mouth or throat in both women and men.”

“There are about 26,000 of these cancers each year—and most could be prevented with HPV vaccine. “

“There are also many more precancerous conditions requiring treatment that can have lasting effects.”
HPV Prophylactic Vaccines

• Made from recombinant L1 capsid proteins that form “virus-like” particles
• These “virus-like” particles **CAN NOT** cause infection with HPV or cause cancer
• **HPV vaccines produce a better immune response than HPV infection**
  – Vaccines produce higher levels of neutralizing antibodies
  – Inactivated so the vaccine can be administered to immuno-compromised individuals
So how can we help reduce the rate and complications of HPV infection?

• **Give a strong recommendation and good screening**
  – How often do you get a chance to prevent cancer?

• **Start the conversation early**
  – Give info & vaccinate before sexual experimentation begins
  – Preteens exhibit a better antibody response

• **Offer a personal story**
  – Patients/Parents typically trust advice from their provider

• **Welcome questions from parents and teens**
  – Especially about safety
    • Remind them that HPV vaccine is safe
    • Vaccination is **NOT** associated with increased sexual activity

Adapted from: www.cdc.gov/vaccines
Can HPV vaccines prevent oral HPV and oropharyngeal cancers?

- It is possible that HPV vaccines might prevent oropharyngeal cancers, since vaccines prevent initial infection with HPV types that cause oropharyngeal cancers.
- Current HPV vaccines were specifically developed to prevent cervical and other less common genital cancers.
- Whether HPV vaccines specifically prevent oropharyngeal cancers has not been studied.

www.cdc.gov/std/hpv/stdfact-hpvandoralcancer.htm
## Available HPV Vaccines

<table>
<thead>
<tr>
<th>Name</th>
<th>Bivalent 2vHPV (Cervarix)</th>
<th>Quadrivalent 4vHPV (Gardasil)</th>
<th>9-Valent 9vHPV (Gardasil 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1 major capsid protein, virus like particle types</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>Licensed for</td>
<td>Females 9-25 years</td>
<td>Females 9-26 years</td>
<td>Females 9-26 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Males 9-26 years</td>
<td>Males 9-15 years*</td>
</tr>
<tr>
<td>Schedule (IM)</td>
<td>3 dose series</td>
<td>3 dose series</td>
<td>3 dose series</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>GlaxoSmithKline</td>
<td>Merck</td>
<td>Merck</td>
</tr>
</tbody>
</table>

ACIP recommended use of 9vHPV in the currently recommended age groups
- At the time of the first application to the FDA, 9vHPV trials in males 16-26 years had not been completed
- Immunogenicity data for males 16-26, reviewed by ACIP has been submitted to the FDA

ACIP Recommendation and AAP Guidelines for HPV Vaccine

• Routine HPV vaccination:
  – recommended for **all** 11-12 year olds
    • males and females

• Catch-up:
  – ages 13-21 years for males
  – ages 13-26 for females

• Permissive use:
  – ages 9-10 years for both males and females
  – ages 22-26 for males

* CDC Advisory Committee on Immunization Practices
* American Academy of Pediatrics
HPV Vaccination

• There is no cure for the HPV virus
• Original vaccine clinical trials focused on cervical cancers
• The FDA restricts from advertising off-label effects
• However, since vaccines prevent cancer causing HPV strains, it’s not much of a scientific leap to extrapolate that
  – “if you can't get the virus, you can't get the things the virus might cause”
• The scientific/medical/dental communities strongly recommend vaccinating to protect from cancers associated with HPV

• Quite Simply, this is an Anti-Cancer Vaccine

http://www.oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php#sthash.QcCCL0uf.dpuf
Talking Tips. . .

• “HPV vaccine is very important because it prevents cancer.”
• “I want your child to be protected from cancer.”
• “That’s why I’m recommending that your daughter/son receive the first dose of the HPV vaccine series today.”

www.cdc.gov/vaccines/youarethekey
HPV Vaccine Safety

• In general, the most common adverse events reported are considered mild
• For serious adverse events reported, there is no unusual pattern or clustering suggesting that the events were caused by the HPV vaccine
• These findings are similar to the safety reviews of MCV4 and Tdap vaccines in adolescents
• 57 million doses of HPV vaccine have been distributed in the US since 2006
• More than 175 million distributed worldwide

www.cdc.gov
Rationale for vaccinating early: Protect prior to HPV exposure

HPV Vaccine in NH Teen Females (13-17 yo)

* Series Complete: Percent of females who received 3 doses among those who had at least 1 HPV dose and at least 24 weeks between the first dose and the interview date.

National Immunization Survey 2013, (Teen, 13-17 years) United States, NH results.

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HPV Vaccine in Teen Females (13-17 years old)

Series complete:
- NH: 67%
- US: 70%

* Series Complete: Percent of females who received 3 doses among those who had at least 1 HPV dose and at least 24 weeks between the first dose and the interview date.

National Immunization Survey 2013, (Teen, 13-17 years) United States, NH results.
HPV Vaccine in Teen Males (13-17 years old)

Series complete:

NH 54.5%
US 48.3%

* Series Complete: Percent of females who received 3 doses among those who had at least 1 HPV dose and at least 24 weeks between the first dose and the interview date.

National Immunization Survey 2013, (Teen, 13-17 years) United States, NH results.
“I’ll pause for a moment so you can let this information sink in.”
Nationally Estimated Vaccination Coverage Levels among Adolescents 13-17 Years, (National Immunization Survey-Teen, 2006-2012)

Reprinted with permission from: www.cdc.gov/vaccines
“HPV coverage remains a problem”
(Anne Schuchat, MD, Asst. Surgeon General)

- 1st dose, girls 13-17 = 57%
- Trails other recommended childhood vaccines by 20-25%
- Currently 4 of 10 girls have not started series
- Intimidating 3 dose schedule
- Ongoing clinical trial testing 2-dose schedule for 9-valent vaccine (undergoing ACIP review)

The Need for HPV Prevention

- Currently only 4 in 10 female American teenagers receive the HPV vaccine
- in Europe, the rate is closer to 8 in 10
- the U.S. has been reluctant to catch up for several reasons:
  - some insurance providers don’t cover the vaccine (not an issue in New Hampshire)
  - people like to think that adolescents aren’t having sex, and therefore don’t need it

www.cdc.gov/vaccines/youarethekey
Dramatic Results in Post-Market “Real-World” Surveillance

• Despite only 33% of girls in US receiving 3 doses
  – 56% reduction in adolescent girls in prevalence of strains 6, 11, 16 & 18 (National Health & Nutrition Examination Study)
  – 77% reduction in Australia (w/in 3 years of 3 doses)
  – 75% reduction in low-grade cervical abnormalities in Australian girls younger than 18 yo (3 doses)
  – 45% reduction in genital warts in Danish girls (16-17 yo)
  – 36% reduction in genital warts in US girls (15-19 yo) (despite low immunization rates)
  – 88% reduction in genital warts in Australian females less than 21 years old
So how do we effectively deliver the facts and discuss Human Papilloma Virus with patients?
Why aren’t more teens vaccinated against HPV?

- CDC Researchers reviewed 55 relevant articles appearing in 2009 or later:
  - Patients cite needing more information
  - Concerns about effects on sexual behavior
  - Patients believe that they are at low risk of HPV infection
  - Social influences
  - Irregular preventive care
  - Vaccine cost

[Photo from www.vmh.com]
Why the need to educate?

• Some patients believe that they/their children won't be exposed to HPV because they aren't sexually active or may not be for a long time
  – “In focus groups, some patients couldn’t understand how they could become infected even if they waited until marriage to have sex.”
  – “Some patients stated that they didn’t think HPV infection was very common because they had never heard that it was or didn’t know anyone who had an HPV infection or HPV disease.”

www.cdc.gov/vaccines/youarethekey
Complications of HPV Infection

If trends continue, the annual number of HPV-positive oropharyngeal cancers is expected to surpass the annual number of cervical cancers by the year 2020.

*This is no longer just a women’s healthcare issue!*
Avoid missed opportunities

– Review immunization records & educate at every visit
  • Acute/well child visits, **dental visits**, sports/camp physicals

– HPV vaccine is safely given with the other recommended adolescent vaccines
  • Best recommendation is one that bundles all indicated adolescent vaccines

– Determine what works best for your practice
  • Have a well-coordinated strategy
  • In medical practices, schedule next HPV vaccine visit before patients leave the office or clinic
  • Utilize reminder/recall strategies to ensure return for remaining doses
What makes HPV such a hot topic?

“The rising incidence of oropharyngeal cancer (specifically oropharyngeal squamous cell carcinoma) associated with HPV is a significant concern for the health care community.”

ADA Council on Scientific Affairs:
Statement on Human Papillomavirus and Squamous Cell Carcinomas of the Oropharynx
Conclusions about HPV Vaccination

• Welcome ?’s from patients, teens and parents
• Educate that almost everyone gets HPV infection

MUST EMPHASIZE THAT HPV IS NOT JUST FOR
WE MUST EMPHASIZE THAT HPV IS NOT JUST FOR

• Give strong recommendations & concrete reasons for getting HPV vaccine

• Inform patients that HPV causes a variety of cancers in women and men

• Remind patients that HPV vaccine is for cancer prevention

• Listen carefully to patient concerns

• See that oropharyngeal HPV is a growing problem
Thank you!