SEXUALLY TRANSMITTED DISEASES AND DENTISTRY: HPV AND OROPHARYNGEAL

BY

DOCTOR DEBORAH SAUNDERS

TUESDAY, MAY 28, 2019 FROM 1:30 P.M. TO 4:00 P.M.

ROOM 517B

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Sexual Health in Oral Oncology

Breaking the news to patients with human papillomavirus-positive oropharyngeal cancer

Deborah P. Saunders, BSc. DMD
Medical Director, Department of Dental Oncology, Medical Lead, Clinical Tobacco Intervention Program, Northeast Cancer Center, Health Sciences North, Assistant Professor, Northern Ontario School of Medicine
THIS PRESENTATION IS CONTROVERSIAL
and MAY BE OFFENSIVE TO SOME AUDIENCES

VIEWER DISCRETION IS ADVISED
Male HPV-related oral cancer rates on the rise: Canadian Cancer Society

Canadian Cancer Society calls on provinces and territories to expand free HPV vaccination programs to boys

Terry Patterson was 49 when he was diagnosed with a tumour on his tonsil caused by HPV. He is advocating for young people to get vaccinated against the virus. (Hannah Yoon/Canadian Press)

Mouth and throat cancers now represent about a third of cancers induced by HPV in Canada, according to a new report.
Recovering: Douglas and wife Catherine Zeta-Jones. The actor was diagnosed with throat cancer in 2010.
Michael Douglas Regrets Attributing His Cancer to His Wife's Vagina

Gabrielle Bluestone
06/29/15 04:16PM Filed to: SEX
• HPV is the most commonly transmitted STI in the world
• 75% of sexually active men and women in Canada will be infected with at least one strain in their lives
• HPV accounts for 5.2% of world wide cancer burden
• In Canada, 2/3 of HPV associated cancer are non-cervical

Population-level incidence of HPV-positive oropharyngeal cancers: increased by 225% (95% CI, 208% to 242%) from 1988 to 2004 (from 0.8 per 100,000 to 2.6 per 100,000).

Incidence for HPV-negative cancers declined by 50% (95% CI, 47% to 53%; from 2.0 per 100,000 to 1.0 per 100,000).

If recent incidence trends continue, the annual number of HPV-positive oropharyngeal cancers is expected to surpass the annual number of cervical cancers by the year 2020.
The rise in incidence of HPV-related OPC makes it now the most common HPV related malignancy in the United States


HPV causes 6 types of cancer

35% of HPV cancers are in the cervix

SOURCE: Canadian Cancer Society, based on 2012 data
1 in 3 newly-diagnosed case of HPV cancers is in men

4 in 5 newly-diagnosed cases of HPV mouth and throat cancers are in men

SOURCE: Canadian Cancer Society, based on 2022 data
4,375 Canadians will be diagnosed with an HPV cancer in 2016.

Only 6 provinces have committed to comprehensive school-based HPV vaccination programs for boys.

SOURCE: Canadian Cancer Society, based on 2016 data
Patients affected are typically in their fifth or sixth decade of life, have an earlier sexual debut, and a higher number of lifetime oral and vaginal sex partners than those affected by HPV-negative OPC.


In addition, these individuals are more often male, of higher socioeconomic status, and less likely to have a history of tobacco or alcohol abuse.
Oral HPV infection is the primary risk factor for HPV-related OPC, and over 90% of oral HPV infections are sexually acquired.

• Therefore, it is no surprise that the number of oral sexual partners is the behavioral factor most strongly and specifically associated with OPC.
• Differences in sexual behavior between countries may contribute to the differences in global trends of HPV-related OPC.

Review

Oropharyngeal squamous cell carcinoma: A unique disease on the rise?

Hester S. van Monsjou *, Alfons J.M. Balm *, Michiel M. van den Brekel *, Volkert B. Wresemann ***,

* Department of Head and Neck Surgery and Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands
** Department of Otorhinolaryngology, Academic Medical Center, Amsterdam, The Netherlands

SUMMARY

Despite successful efforts to control tobacco and alcohol consumption in the Western world, several developed countries report rising oropharyngeal squamous cell carcinoma (OPSCC) incidence figures, specifically in young individuals. Similar to anogenital cancers, a significant proportion of OPSCC (up to 60%) is caused by sexually acquired HPV infection and the rise in OPSCC has been attributed to changing sexual behaviours in the Western World. Accordingly, patients with HPV-positive OPSCC report divergent sexual histories and absence of classical risk factors as tobacco and alcohol exposure compared to patients with HPV-negative OPSCC. The profile of HPV-positive OPSCC differs from HPV-negative OPSCC in several other significant aspects, including a unique molecular biologic tumor characteristics and improved clinical behaviours. Thus, a further increase in HPV-positive OPSCC will impact significantly upon clinical management of OPSCC unless it is halted by adequate preventive measures aimed at reduction of HPV-associated disease. HPV vaccination has been recently offered to young females in an attempt to reduce HPV-induced cervical cancer and may ultimately result in a decline of OPSCC incidence as well. Until then, close collaborations between otolaryngologists/head and neck surgeons and anogenital/gynaecological specialists is warranted to optimise clinical management of HPV-induced malignancy and improve detection of second primary tumor development.

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Figure 1 Geographic distribution of head and neck cancer. Estimated age-standardized incidence rate per 100,000, both sexes, all ages, 2008.

In addition to viral exposure, concomitant tobacco use may also play a part in the development of HPV-related OPC.
The Virus
• HPV is a double-stranded DNA virus with predilection for squamous epithelium.
• Cryptic epithelium overlying the tonsils and tongue base acts as a reservoir for the virus, providing access to its basal layer for viral replication.

Over time, malignant transformation can occur when viral oncoproteins disrupt tumor suppression genes in native tissue.
• Reticulated crypt epithelium in the oropharynx is unique to this anatomical location in the head and neck, and may explain why HPV is estimated to be five times higher in the oropharynx when compared to the oral cavity, larynx, or hypopharynx.

• Although there are many types of HPV, the overwhelming majority of HPV-related OPC cases are caused by HPV16.
HPV Infection

Langerhans cells

Dendritic cells

Dermis

Non-responding HPV-specific T cells

Micro-wound

CD 16

Epidermis

Basement membrane

Dermis

Draining lymphatics
Mechanisms of HPV Transmission and Acquisition

- **Sexual contact**
  - Through sexual intercourse
  - Genital–genital, manual–genital, oral–genital
  - Genital HPV infection in virgins is rare, but may result from nonpenetrative sexual contact.
  - Condom use may help reduce the risk, but it is not fully protective.

- **Nonsexual routes**
  - Mother to newborn (vertical transmission; rare)
  - Fomites (eg, undergarments, surgical gloves, biopsy forceps)
    - Hypothesized but not well documented
HPV subtypes & disease

• HPV over 100 subtypes
• HPV 6, 11 most common - non oncogenic
  – Genital/anal warts
  – Laryngeal papillomas
• HPV 16, 18 – oncogenic
  – Cervical cancer (70%), VIN, VAIN in women
  – Penile cancer in men
  – Oral and anal cancer in men and women
  – HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Jit BMJ 2011;343:5775 & Johnson et al STI 2012;88:212-17
Heck’s Disease HPV 13
Squamous Papilloma, Verruca Vulgaris, Condyloma Acuminatum HPV 6,11
Squamous Cell Carcinoma HPV 16
Malignant Transformation
Annual Cancer Statistics: Oral and Pharyngeal Cancer

- Worldwide: 3\textsuperscript{rd} most common cancer
  - 560,000 cases 2002; 298,000 deaths
- US: 6\textsuperscript{th} most common cancer
  - 1:10,000 adults; 79 new cases per day; 1 death/hour
  - 46,000/yr; ~10,000 deaths
- Overall 5 yr survival:
- 2/3 present with advanced stage disease
- OPC: HPV in up to 85% cases

• HPV-induced Carinogenesis (p53 and pRb)
  • E7 protein from the HPV virus leads to inactivation of TP53 and Rb gene leading to chromosomal instability which contributes to tumor progression

• Tobacco/Alcohol-Related Carcinogenesis (DNA)
  • Tobacco carcinogenesis combined with alcohol use causes mutations that silence the TP53 tumor suppressor gene
  • Tobacco carcinogens cause mutations that inactivate the P16 gene which lies upstream of the Rb tumor suppressor gene. This silencing of the P16 gene inactivates Rb leading to chromosomal instability
Low prevalence of Human Papillomavirus in oral cavity carcinomas

Jerry Machado,1,2 Patricia P Reis,2 Tong Zhang,2 Colleen Simpson,3 Wei Xu,4 Bayardo Perez-Ordónez,5 David P Goldstein,3 Dale H Brown,3 Ralph W Gilbert,3 Patrick J Gullane,3 Jonathan C Irish,3 and Suzanne Kamel-Reid 1,2,6,7
Available at http://www.cancercare.on.ca/cancerfacts.

Source: Cancer Care Ontario (Ontario Cancer Registry, 2010)
*HPV-related cancers: squamous cell carcinomas of the base of tongue, lingual tonsil, tonsil oropharynx, and Waldeyer ring (C019, C024, C090–C109, C142)
**HPV-unrelated cancers: squamous cell carcinomas of the tongue, gum, floor of mouth, palate, other & unspecified parts of the mouth (C020–C023, C025–C069)
+Squamous cell histologies: ICD-O-3 8050–8076, 8078, 8083–8084, 8094
PMH series (2001-2009): 81% (308/382) HPV(+) were stage IV

<table>
<thead>
<tr>
<th>Outcome at 3-years (n=505)</th>
<th>HPV-related (n=382)</th>
<th>Smoking-related (n=123)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>83%</td>
<td>49%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Local Control</td>
<td>94%</td>
<td>80%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Regional Control</td>
<td>95%</td>
<td>82%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Distant Control</td>
<td>90%</td>
<td>86%</td>
<td>0.530</td>
</tr>
<tr>
<td>Late Toxicity</td>
<td>17%</td>
<td>34%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Loco-regional Control**

91% vs 68% at 5-years, p<0.001

**Distant Control**

87% vs 86% at 5-years, p=0.530
• HPV-positive OPC is linked with a more favorable prognosis, but with high recurrences within two years of diagnosis when compared to HPV-negative disease [10,11]
ATYPICAL CLINICAL BEHAVIOR OF p16-CONFIRMED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA Treated by Radical Radiotherapy


Shao Hui Huang,‡ Bayardo Perez-Ordonez,‡, Ilan Weinreb,‡, Andrew Hope,‡, Christine Massey,¶, John N. Waldron,§, John Kim,‡, Andrew J. Bayley,§, Bernard Cummings,§, B.C. John Cho,§, Jolie Ringash,¶, Laura A. Dawson,¶, Lillian L. Siu,¶, Eric Chen,¶, Jonathan Irish,¶, Patrick Guilleane,¶, Angela Hui,¶, Fei-Fei Liu,¶, Xiaowei Shen,¶, Wei Xu,¶, Brian O’Sullivan,¶"HPV(+) DM: Two Phenotypes:

- "disseminating" phenotype: "explosive" character
- "indolent" phenotype with longer term survival
- potentially curable!!!
Human Papillomavirus–Positive Oral Cavity and Oropharyngeal Cancer Patients Do Not Have Better Quality-of-Life Trajectories

Arun Sharma, MD, MS\(^1\), Eduardo Méndez, MD, MS\(^{1,3}\), Bevan Yueh, MD, MPH\(^4\), Pawadee Lohavanichbutr, MD\(^5\), John Houck\(^5\), David R. Doody, MS\(^3\), Neal D. Futran, MD, DMD\(^1\), Melissa P. Upton, MD\(^4\), Stephen M. Schwartz, PhD, MPH\(^5,7\), and Chu Chen, MS, PhD\(^1,5,7\)

Figure 1. Relationship between HPV DNA status and QOL in OSCC patients, University of Washington Affiliated Hospitals, Seattle, Washington, 2003-2010.

Immediate posttreatment: data collected 3 to 8 months after treatment started.

One-year posttreatment: data collected 9 to 15 months after treatment started.

Abbreviations: HPV, human papillomavirus; OSCC, oral cavity and oropharyngeal squamous cell carcinoma; QOL, quality of life.
Concurrent Chemo-radiotherapy: Late Toxicity

- Analysis of 230 patients receiving CRT in 3 studies (RTOG 91-11, 97-03, 99-14)

![Bar chart showing percentages of patients experiencing different toxicities.]

- Any severe late toxicity: 43%
- Feeding-tube dependence >2 yrs post-RT: 13%
- Pharyngeal dysfunction: 27%
- Laryngeal dysfunction: 12%
- Death: 10%

*Slide courtesy of Prof Jan Vermorken*

“We’ve found a mass. The good news is we have weapons of mass destruction.”
Oropharyngeal Carcinomas (OPC)

- Soft palate
- Palatine and lingual tonsils
- Base of tongue
- Surrounding tissues
Signs and Symptoms of OPC
Signs and Symptoms of HPV OPC

- Lymphadenopathy of neck ****
- Difficulty swallowing persistent over 3 weeks
- “Hot potato syndrome”
- Sore throat, swelling of throat, enlarged tonsils +/- tonsillectomy
- Radiating pain to the ear (otalgia)
Oral Squamous Cell Cancer, Oropharyngeal Cancer

- OSCC: often detectable mucosal changes prior to progression to SCC:
  - leukoplakia
  - erythroplakia
  - mixed lesions
- OPC: detectable premalignant change?
- Molecular testing possible?
  - saliva biomarkers, cells, biopsy
  - HPV testing
• The lack of an identifiable early lesion presents a significant challenge when evaluating for premalignant and malignant lesions of the oropharynx
• However, unlike the Papanicolaou test for cervical cancer, there is no current reliable screening method to detect precancerous OPCs.
Challenges to screening include lack of a precursor lesion and a long latency period between exposure to virus and onset of disease.
Oral HPV Screening

- An initial approach considered for assessment was to use oral HPV screening. This technique evaluates for the presence of HPV DNA in saliva and can be even used to focus specifically on high-risk HPV such as HPV 16. However, while this technique can be effective in demonstrating active HPV infection, it is of little utility in screening for HPV-related OPC as the majority of individuals either go on to clear the infection or fail to progress to malignancy. Consequently, the use of oral HPV screening has been discouraged as a screening technique to identify OPC.55
HPV serology One area that has shown particular promise in assessing high risk populations is to screen for serum antibodies to HPV 16 proteins. Such an approach may allow for at-risk individuals to be identified prior to progression of disease. In an early study by Mork et al., serum positivity to the L1 capsid protein of HPV 16 conferred a 14-times increased risk of developing OPC, when linking findings from a Nordic serum bank and tumor registries.56
While these findings were encouraging, these antibodies represent the body’s cumulative exposure to HPV16 and are not specific to anatomic site. Moreover, they do not reflect expression of HPV oncoproteins necessary for carcinogenesis.
• In 2013, Kreimer and colleagues identified that serum antibodies to the E6 oncoprotein of HPV 16 were a better marker for predicting cancer.38
• In addition to assessment of nodal disease, the use of transcervical ultrasound has now been applied to evaluate the oropharynx in an effort to identify occult tumors, especially those developing in crypts of the palatine and lingual tonsils, not visible on surface examination.59,60

Mucosal Imaging

- Narrow band imaging (NBI) and endoscopic lifetime-resolved laser – induced imaging


Serum Markers

• Virally mediated cancers are particularly well suited for such “liquid biopsies” as they have known viral DNA incorporated into the host DNA that can be queried.

• This approach has demonstrated tremendous promise in screening for Epstein-Barr virus (EBV)-related nasopharyngeal cancer.

Despite their promise, all mucosal imaging techniques have limitations in OPC screening as many tumors originate in the depths of tonsillar crypts and thus are not well seen on surface evaluation.
Risk Factors
<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Young age (peak age group 20–24 years of age)¹</td>
<td>• Young age (peak age group 25–29 years of age)¹</td>
</tr>
<tr>
<td>• Lifetime number of sex partners²</td>
<td>• Lifetime number of sex partners⁶</td>
</tr>
<tr>
<td>• Early age of first sexual intercourse³</td>
<td>• Being uncircumcised (?)⁶</td>
</tr>
<tr>
<td>• Male partner sexual behavior³</td>
<td></td>
</tr>
<tr>
<td>• Smoking⁴</td>
<td></td>
</tr>
<tr>
<td>• Oral contraceptive use⁴</td>
<td></td>
</tr>
<tr>
<td>• Uncircumcised male partners⁵</td>
<td></td>
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</tbody>
</table>

# Prevalence of HPV Infection in Young Men

<table>
<thead>
<tr>
<th>Study Author, Year</th>
<th>N</th>
<th>Selected Age Range (Years)</th>
<th>HPV Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baldwin, 2004* †</td>
<td>393 †</td>
<td>18–24</td>
<td>34%</td>
</tr>
<tr>
<td>Weaver, 2004²</td>
<td>317</td>
<td>18–25</td>
<td>33%</td>
</tr>
<tr>
<td>Svare, 2002* ‡</td>
<td>44</td>
<td>18–24</td>
<td>48%</td>
</tr>
<tr>
<td>Kataoka, 1991³</td>
<td>108</td>
<td>18–23</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Conducted at a sexually transmitted disease clinic
† Number includes all patients included in the study (18–70 years of age).

Giving oral sex on an HPV-infected penis, vagina or genital area can result in an HPV throat infection (> anilingus)

Getting oral sex from a partner with HPV in the throat may results in getting HPV on the genital area, anus or rectum.

HPV may not be found until many years after exposure; therefore, not helpful (or fair) to blame your partner.
Dictionary of Terms

**Fellatio (Blow Job)**
Using lips, mouth or tongue to stimulate the penis

**Cunnilingus (Going Down On)**
Using lips, mouth or tongue to stimulate the vagina

**Anilingus (Rimming)**
Using lips, mouth or tongue to stimulate the anus
OMG – did she actually just say that @ JDIQ?
• Bonus question
Oral lichen planus: malignant transformation and human papilloma virus: A review of potential clinical implications

Meir Gorsky, DMD, a and Joel B. Epstein, DMD, MSD, FRCD (C) FDS RCSEd,b Tel Aviv, Israel, and Chicago, IL TEL AVIV UNIVERSITY AND UNIVERSITY OF ILLINOIS

Oral lichen planus (OLP) occurs in from 2% to 3% of the population and may have a risk of malignant transformation into squamous cell carcinoma (SCC). This risk is not necessarily associated with exposure to tobacco and alcohol. An increased awareness of a possible role of human papilloma virus (HPV) and SCC led us to review a possible association between this virus infection and malignant transformation of OLP. The possible linkage between HPV and the risk of transformation of OLP to malignancy is discussed. Furthermore, management of OLP using immunosuppressive drugs may be associated with enhanced viral replication and could theoretically affect the risk of malignant transformation. Implications for clinical care are discussed. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:461-464)
Why Now?
Why Now?

- Oral Contraceptives and Condoms
- Changes in Sexual Norms/Practices
  - Sense of Invincibility
- Lack of Awareness
Sexual Revolution
Sexual Landscape: Straight and Gay
Condom Use
Changes in the Gay Community

Proportion of men reporting activities which could transmit HIV

- 2006: 25%
- 2007: 37%

Proportion of gay men who have never had an HIV test

- 2006: 11%
- 2007: 17%

Sex Now Survey
Based on a survey of 1533 BC men who completed Sex Now 2007
How Common is Oral Sex?

• **More than 85%** of sexually active adults reported having oral sex at least once with a partner of the opposite sex

• **33%** of teenage boys and girls aged **15-17** reported having had oral sex with a partner of the opposite sex
Is Oral Sex Safer than Vaginal or Anal Sex?

- Difficult to compare exact risks (think about it)

- Risk of getting HIV from oral sex with an infected partner is much lower than the risk of getting HIV from anal or vaginal sex. However…..

This may not be true for other STDs
Why Mostly Men?
HPV Clearance

- In women 15–25 years of age, ~80% of HPV infections are transient.¹
  - Gradual development of cell-mediated immune response

- 70% of new HPV infections cleared within 1 year and 91% within 2 years.³
  
  Median duration of infection = 8 months³


• The oral HPV prevalence in women with cervical HPV infection is low.

• The data suggest that HPV transmission to the oropharynx represents a rare and unlikely event. Knowing that vaginal sexual intercourse represents the main risk factor for cervical HPV infection, oral sexual practice seems to have less importance to oropharyngeal HPV infection.

• Routine testing for oral HPV Infection in women with cervical HPV infection and their sexual partners does not seem feasible as a screening strategy for oropharyngeal squamous cell carcinoma at the moment.
Sex Differences in Risk Factors and Natural History of Oral Human Papillomavirus Infection

Gypsyamber D’Souza,1 Alicia Wentz,1 Nicole Kitz,1 Yuxian Zhang,1 Elizabeth Sugar,1 Renee M. Youngblood,2 Yingshi Guo,2 Weihong Xiao,2 and Mauren L. Gillison2

1Johns Hopkins Bloomberg School of Public Health, and 2Baltimore County Health Department, Maryland; and 3Ohio State University Comprehensive Cancer Center, Columbus

Oral human papillomavirus genotype 16 (HPV16) infection causes oropharyngeal squamous cell carcinoma (SCC), and the prevalence of oropharyngeal SCC is higher among men than women in the United States. In a cohort study of oral HPV infection among 409 individuals aged 18–25 years, the risk among men but not among women significantly increased as the number of recent (ie, within the prior 3 months) oral sex partners increased ($P_{\text{interaction}} = .05$). In contrast, the risk among women but not among men significantly decreased as the lifetime number of vaginal sex partners increased ($P_{\text{interaction}} = .037$). Men were also significantly less likely than women to clear oral HPV infection. Our data contribute to understanding sex differences in risk for HPV-positive oropharyngeal SCC.
HPV Vaccination and Immunity
GAME CHANGE?
• The oral HPV prevalence in women with cervical HPV infection is low.

• It has been estimated that, by vaccinating boys and men, 5416 and 51,168 additional cases of HPV-related OPC would be prevented at 50 and 100 y, respectively.
There's growing evidence that the virus that causes cervical cancer in women is also linked to cancers in men, leading health professionals to call for an HPV vaccination program for boys.

[...]
Recent research found more than half of some oral cancers in men are associated with the HPV. While many Canadian provinces fund programs to vaccinate girls against HPV to prevent cancer, there are none for boys.  

[...]
However, while cervical cancer is the second most common cancer in women, oral cancers linked to HPV are estimated to affect a relatively small number of men — hundreds a year in Canada.

Health Canada has not approved the HPV vaccine for boys or men. But the company that makes Gardasil is testing it on men now.
<table>
<thead>
<tr>
<th></th>
<th>Cervarix</th>
<th>Gardasil</th>
<th>Gardasil 9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>Females Only</td>
<td>Females and Males in the US Females only in the UK</td>
<td>Females and Males in the US</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>9-25</td>
<td>9-26</td>
<td>Females 9-26 and Males 9-21</td>
</tr>
<tr>
<td><strong>Recommended Age at Vaccination</strong></td>
<td>11-12 in the US 12-13 in the UK</td>
<td>11-12 in the US 12-13 in the UK</td>
<td>11-12 in the US</td>
</tr>
<tr>
<td><strong>HPV Strains the Vaccine Covers</strong></td>
<td>HPV-16 and HPV-18</td>
<td>HPV-6, 11, 16 and 18</td>
<td>HPV-6, 11, 16, 18, 31, 33, 45, 52, and 58</td>
</tr>
<tr>
<td><strong>Protects Against</strong></td>
<td>Cervical Cancer</td>
<td>Anal, Cervical, Vulvar and Vaginal Cancer; Anogenital Warts; Vaginal, Vulvar, Cervical and Anal Intraepithelial Neoplasia</td>
<td>Anal, Cervical, Vulvar and Vaginal Cancer; Anogenital Warts; Vaginal, Vulvar, Cervical and Anal Intraepithelial Neoplasia</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>3 over 6 month period</td>
<td>3 over 6 month period</td>
<td>3 over 6 month period</td>
</tr>
</tbody>
</table>
Gardasil or Gardasil 9?

1. **Why do we care?** Infection with human papillomavirus (HPV) types 16, 18, 31, 33, 45, 52, and 58 is implicated in 90 percent of cervical cancers. **Gardasil 9** targets those seven listed above, in addition to the two types associated with genital warts (6 and 11).

2. **Is Gardasil 9 better than the quadrivalent HPV vaccine (Gardasil) we’ve been using?** Immune response to the two vaccines are similar for the HPV types targeted by both (6, 11, 16, and 18). **Gardasil 9 is also 97 percent effective for preventing precancerous and cancerous lesions of the cervix and vagina associated with the other targeted HPV types (31, 33, 45, 52, and 58).** Hence, the **Gardasil 9** is favored for its broader HPV coverage.
3 When should you get Gardasil 9? Immunization should be offered to boys and girls ages eleven to twelve, but can be administered as early as nine years of age. Catch-up vaccination should be offered for guys between the ages of 13 to 21 and girls between 13 to 26 years who have not been vaccinated.

4 If I had the Gardasil vaccinations already, do I get the new one? No. Re-vaccination with Gardasil 9 is not warranted for those who have completed the series with a different HPV vaccine.
5 The girls. To summarize the recommendation for girls: either the quadrivalent or *Gardasil 9* HPV vaccine is recommended for the prevention of anal cancer, cervical cancer and its precursor lesions, and genital warts in females. Again, the newer *Gardasil 9* is preferred given its greater HPV type coverage.

6 I’ve already had HPV infection, will the vaccine help? Neither vaccine treats or accelerates the clearance of pre-existing HPV infections.
What if I’ve already had an abnormal pap from HPV? Females who are sexually active should still be vaccinated consistent with age-specific recommendations and a history of an abnormal pap, genital warts, or HPV infection is NOT a contraindication to the vaccine. Having said that, Gardasil vaccine is less beneficial for females who have already been infected with one or more of the HPV vaccine types.

The guys. Gardasil 9 is also recommended over the quadrivalent vaccine (Gardasil) for males given its greater HPV type coverage.
Why vaccinate the boys if the girls are vaccinated? Several reasons:

- Immunization rates in young girls are generally low so vaccinating males will help prevent infection in unimmunized females.

- Gardasil 9 vaccination will protect against HPV-related infection and disease in men who have sex with men.

- HPV infection is common in males and is readily transmitted, influencing disease infection rates in both males and females.
Does the **Gardasil 9** vaccine prevent HPV related head and neck cancers? We don’t know yet. While the **Gardasil 9** works to prevent 93% of oral HPV, whether HPV vaccination can prevent the development of HPV-related head and neck cancer has not yet been evaluated.
HPV Vaccine Safety

• Reviewed by multiple regulatory agencies globally including WHO, US Food and Drug, Health Canada, CDC and Global Advisory Committee on Vaccine Safety

• No serious side-effects reported in large clinical trials, conducted on Cervarix, Gardasil and Gardasil-9

• No evidence of neurological or autoimmune diseases; no deaths directly attributable to HPV vaccination
Vaccine Safety

Australian Data (7 million doses)

1,991 suspected Adverse Events

- Headache 388 (19.5%)
- Injection Site Pain 364 (18.3%)
  - Dizziness 282 (14.2%)
- Fatigue/Lethargy 217 (10.9%)
  - Fever 212 (10.6%)
  - Fainting 171 (8.6%)
  - Vomiting 165 (8.3%)
- General Feeling of Unwell 162 (8.2%)
HPV Vaccine and Risk of MS

Denmark, Sweden ~ 4M females studied

- 789K with vaccine; 1.9M vaccine doses
- During 10 yr follow up, 4322 cases of MS; 3300 of other demyelinating diseases
- In cohort, no increased risk of diseases in vaccinated population
- Findings do not support a causal relationship between MS and qHPV
PAP Testing After Vaccine?

• Yes, as HPV vaccines protect against most but not all cancers of the cervix

• However, move away from PAP and towards HPV DNA testing (sensitivity) for cervical screening
Success of HPV vaccination is now a matter of coverage

‘...increasing coverage, particularly of the sexually-naïve adolescent females, is now the most important public health issue in HPV vaccine efforts.’

Schiffman et al. Lancet Oncology, 2011
Examined predictors of HPV vaccine uptake in 2010 after launch of school based program

After overall attitudes to vaccines, recommendation of family physician was a main predictor of HPV vaccine uptake
Emerging Issues

• Social Change

• Professional Change

• Health Care Policy

• Education
Vaccination in Canada

• In Canada the National Advisory Committee on Immunization (NACI) issued an update in January 2012 on HPV vaccines, which included recommendations for males ages 9–26 and females aged 9–45

Currently, only the quadrivalent vaccine (Gardasil®), protecting against HPV 6/11/16/18) and (Gardisil®9), protecting against HPV 6/11/16/18/31/33/45/52/58) are recommended for men.
• Publically funded school based HPV vaccination programs are available for both girls and boys in selected provinces and territories across Canada, including Ontario.

Vaccination of Men

- The desire to include men increased based on HPV vaccination rates failing to reach the levels necessary to establish herd immunity, gender equity issues, and a lack of protection for men having sex with men.


Vaccination for all Canadians

• However, outside of school programs, HPV vaccination remains unsubsidized and it is excluded from many other worldwide national immunizations programs.


HPV vaccination in male physicians: A survey of gynecologists and otolaryngology surgeons' attitudes towards vaccination in themselves and their patients

Claire Stanley, Michael Secter, Sarah Chauvin, Amanda Selig

Abstract

Objective: Attitudes and barriers towards HPV vaccination were explored in a population of male physicians in Gynecology and Otolaryngology in Ontario, Canada.

Methods: An interest-based survey was distributed to male residents and physicians affiliated with the departments of Obstetrics and Gynecology, and Otolaryngology at six Ontario universities. The survey consisted of 16 questions (2 demographic, 3 workplace exposure, 6 regarding personal vaccination, and 5 regarding patient vaccination). Subgroup analysis examined differences between residents versus staff physicians and gynecologists versus otolaryngologists.

Results: Most respondents (54/92, 58.6%) had not been vaccinated against HPV, yet would consider vaccination in the future (42/51, 82.4%). Significantly more residents would consider vaccination compared to staff physicians (p < 0.01). Personal promotion from being HPV disease was the most common motivating factor (26/78, 42.4%) among participants. A notable barrier to vaccination was “age over recommendations” (9/44, 20.4%). Most participants would recommend the HPV vaccine to both male patients (40/92, 74.0%) and male partners of female patients (47/62, 75.8%).

Conclusion: This study demonstrates male gynecologists and otolaryngologists had largely favorable attitudes towards HPV vaccination though few had received vaccination. These findings may be used to increase HPV vaccine uptake among male health care professionals and their patients.
Motivation to be Vaccinated or to Consider Vaccination

- (25/59, 42.4%) motivating factor selected among participants was personal protection from benign HPV diseases.
- Potential partner protection from benign HPV disease was the least commonly chosen response (13/59, 22.0%).
Motivation to NOT be Vaccinated or to Consider Vaccination

• “Current age over recommendations” (9/44, 20.4%)
• Personal cost (5/44, 11.4%)
• Low perceived exposure risk
• Most participants (43/60, 71.7%) indicated that financial coverage of the HPV vaccine would make them more likely to seek the vaccination.
Key Messages for Patients
HPV-Positive Oropharyngeal Cancer

Common questions & answers about HPV-positive oropharyngeal squamous cell cancer (HPV-OSCC)

Patient Fact Sheet

What is Human Papillomavirus (HPV)?
- HPV is a common, sexually transmitted infection that can affect the mouth, throat, and skin.
- There are many types of HPV, and different types can cause different infections.
- HPV is the most common STI in Canada. Over 8 million Canadians have been diagnosed with genital or oral HPV infection.

What causes oropharyngeal cancer?
- HPV types most associated with oropharyngeal cancer include HPV-16, 18, and 31.
- Smoking and alcohol use can also cause oropharyngeal cancer.

How did I get oral HPV infection?
- HPV is transmitted through sexual contact. It may also be possible to get oral HPV by other ways, such as oral sex and sexual contact, but these methods are less common.
- Smoking and alcohol use can increase the risk of oral HPV infection.
- HPV can remain in the body for years even after infection has resolved.

Who has oral HPV infection?
- Most people (90% of men and 80% of women) have at least one type of HPV in their bodies. However, HPV can be very common in the body of healthy people.
- Most people who have oral HPV in their bodies never develop oral cancer.

Can I transmit oral HPV infection to others?
- Oral HPV can be transmitted through sexual contact.
- Transmissions can occur during oral sex, kissing, or oral contact with genital HPV.

HPV-OSCC and Genital Cancer
- Oral and genital cancers can occur in the same person.
- Both types of cancer are caused by HPV.

What does having HPV in my bottom mean?
- Most people who have HPV in their bodies do not develop cancer.
- HPV can remain in the body for years even after infection has resolved.

What can I do about oral HPV infection?
- There is no cure for HPV, but there are treatments that can help manage symptoms.
- HPV can be managed through treatment and prevention.

When did I get this infection?
- Most people acquire HPV through sexual contact, but it is not possible to determine when.

Who should be screened for HPV-OSCC?
- People who are at high risk for HPV-OSCC include:
  - People with a history of HPV-OSCC.
  - People with a history of HPV-related head and neck cancer.
  - People with a history of HPV-related laryngeal cancer.
  - People who use snuff or smoke tobacco.

ODA Resources
KEEP CALM AND HAVE SAFE SEX
Human papilloma virus is common.

Most people will clear oral human papillomavirus infection within 1 year

Infectivity of HPV and Partner Consideration

- Immunity to HPV
- Once infected can not get re-infected
- 170 subtypes of HPV, 300 subtypes of cold virus
- Cervical warts, penile warts good indication that individual is a carrier, partner can be immune
Human papillomavirus is transmitted by normal sexual activity.
Oral sex increases the rate of oral HPV infections, but the prevalence of the infection also increases with the number of lifetime or recent sexual partners for any kind of sex.


Normal Sexual Activity

• Oral sex is a normal sexual activity
  • In the US, 80% of sexually active people aged 15-44 have had oral sex with an opposite sex partner

Normal Sexual Activity

- It is also possible that HPV can be transmitted by deep kissing-
data inconclusive


Human papillomavirus may be acquired many years before a cancer develops.


Long-term partners do not seem to be at increased risk of human papillomavirus infection


GYNECOLOGIC ONCOLOGY

Oral Human Papillomavirus (HPV) Infection in HPV-Positive Patients With Oropharyngeal Cancer and Their Partners

Gypsymber D’Souza, Neil D. Gross, Sara I. Pai, Robert Hadidad, Karen S. Anderson, Shirani Rujan,
Jennifer Gerber, Maura L. Gillison, and Marshall R. Posner

Listen to the podcast by Dr D’Souza at www.jco.org/podcasts

ABSTRACT

Purpose
To better understand oral human papillomavirus (HPV) infection and cancer risk among long-term sexual partners of patients with HPV-positive oropharyngeal cancer (HPV-OPC).

Patients and Methods
An oral rinse sample, risk factor survey, cancer history, and oral examination (partners only) were collected from patients with HPV-OPC and their partners. Oral rinse samples were evaluated for 36 types of HPV DNA using PGMY 09/11 primers and line-blot hybridization and HPV16 copy number using quantitative polymerase chain reaction. Oral HPV prevalence was compared with infection among those age 45 to 65 years using National Health and Nutrition Examination Survey (NHANES) 2009-2010.
Oral Human Papillomavirus (HPV) Infection in HPV-Positive Patients With Oropharyngeal Cancer and Their Partners


Listen to the podcast by Dr D’Souza at www.jco.org/podcasts

Conclusion
Oral HPV16 DNA is commonly detected among patients with HPV-OPC at diagnosis, but not among their partners. Partners of patients with HPV-OPC do not seem to have elevated oral HPV infection compared with the general population.
Modification of sexual behavior is not necessary

- Oral rinses of 164 pt HPV+ OPC and 93 partners
- Prevalence high in patients at Dx (HPV:61%, HPV-16:54%)
- Prevalence was significantly lower in their partners (any HPV:1.2%, HPV-16:0%) at levels below those seen in the general population
- No oral abnormalities or precancers were detected on examination in any of the partners


Risk of another human papillomavirus–related cancer is low


Prophylactic vaccines can prevent oral human papilloma virus infection but will not help treat established cancers.

Questions?
Thank you!