

The Role of HPV in Head & Neck Cancer

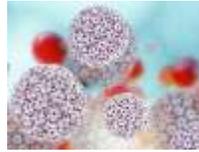
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What is HPV?

- Human Papillomavirus
- Over 150 strains
- Associated with benign or malignant changes
- Benign: warts, papillomas
- Malignant: ~12 strains associated
 - Cancers of the **oropharynx**, sinuses, cervix, vulva, vagina, penis, and anus
 - **Oropharyngeal carcinoma**—HPV causes 70%
 - HPV 16—Over 90%



HPV

- 8 out of 10 will contract HPV
 - Body usually fights off infection
 - Immunocompromised status—> infection
- Can develop symptoms years after being infected
 - Hard to know when you first became infected

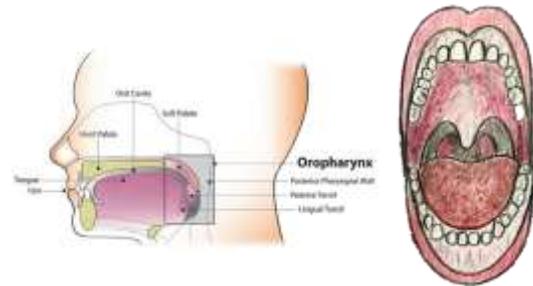


Tappouni, Anwar. Immune Reconstitution Inflammatory Syndrome. *Adv Dent Res.* 23(1):90-6 - April 2011

Head and Neck Squamous Cell Carcinoma (SCC)

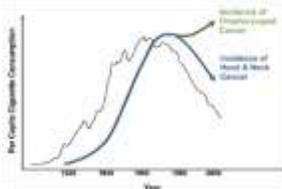
- 600,000 cases worldwide each year
- 40-50% mortality
- Develop in epithelium of mucosal linings of upper airway and food passages
- Risk Factors
 - Smoking
 - Alcohol
 - **HPV**—70% (Oropharynx)
 - Occurs mainly in Western World
- **Divided into HPV+ and HPV- cancers**

Oropharynx

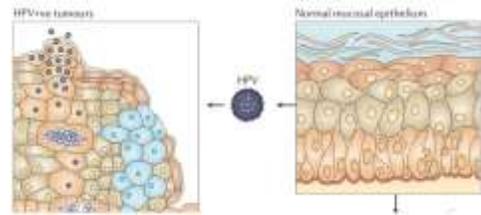


HPV in Head and Neck SCCa

- Highest risk in **middle-aged men**
- 17,500 women and 9,300 men affected by HPV-related cancers in the United States each year
- 225% increase in HPV-positive SCC vs 50% decrease in HPV-negative SCC (SEER 1984-2004)



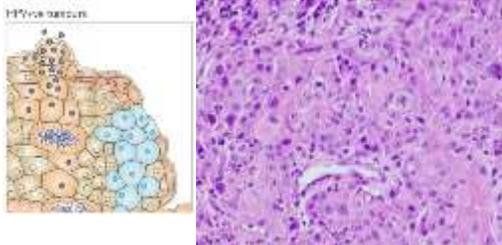
HPV Role in Cancer



Mutations
Chromosomal Losses
Chromosomal Gains

Nature, May 2018

HPV Role in Cancer



REVIEWS

The molecular landscape of head and neck cancer

C. René Lippman¹, Peter J. A. Singer² and Karim H. Al-Sarraf^{1*}

Alterations in head and neck squamous cell carcinoma (HNSCC) genes in the mucosal lining of the upper aerodigestive tract and are consequently heterogeneous in nature. Clinical risk factors are smoking and alcohol consumption, and in recent years, the role of human papillomavirus (HPV) has emerged, particularly in oropharyngeal tumors. HPV-induced molecular changes are consistently repeatable and, by which, mainly by conventional means of progression, shaping a distinct molecular profile of the mucosal lining of the upper aerodigestive tract. However, the recent discovery of HPV in HNSCC has raised the possibility that HNSCC may be a distinct entity, but with some key genetic alterations, analogous to the previous. In 2015, The Cancer Genome Atlas (TCGA) reported on a distinct molecular landscape in HNSCC. The genomic landscape of head and neck cancer is heterogeneous and is characterized by the presence of a subgroup of genetically distinct HPV-negative head and neck tumors with favorable prognosis was confirmed. Tumors can be further subdivided based on genomic profiling. However, the exact clinical implications remain unclear, and requires detailed biological investigation. It also became apparent that HNSCC is a disease that is not defined by repeat mutations that drive oncogenesis, indicating that cancer therapies might be effective in HNSCC. There is a need to understand the role of HPV in HNSCC and to determine whether and how it can be considered as a prognostic factor in head and neck cancer.

Nature, May 2018

HPV Mode of Transmission

- Skin-to-skin, skin-to-mucosa contact
 - Fingers/toes in mouths
 - **Vaginal, oral, and anal sex**
- Pregnant woman to baby
 - Recurrent respiratory papillomatosis (RRP),
 - Warts grow inside the throat



Clinical—HPV Changes

- Leukoplakia—most common
- Erythroplakia
- Mass
- Ulcer



Heathline.com

Oral/Oropharyngeal Exam

- Part of routine oral exam performed by dentists and other practitioners

Oral/Oropharyngeal Exam



Oropharynx:

Visualization

Palpation of posterior lateral and ventral tongue

Symmetry of tonsils and tonsillar pillar

[Oral Exam Youtube Video](#)

High Risk Areas



Refer for evaluation and possible biopsy

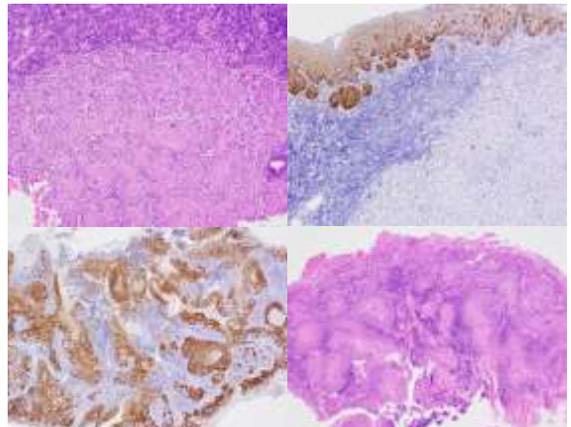


Oral surgeon
Oral Pathologist
Periodontist





Photo courtesy of Dr. Craig Fowler



Treatment

- Early-stage tumors:
 - Surgery or radiotherapy
- Advanced stage tumors:
 - Surgery with postop chemoradiotherapy or
 - Upfront chemoradiation with surgical salvage if possible
- Induction chemotherapy not widespread: lack of benefit in previous studies
- Besides improving patient survival, another major aim of therapy is an improved quality of life

Treatment

- Recent advances:
 - Sentinel node biopsy
 - Transoral robotic resections
 - Image-based and adaptive radiotherapy
 - Application of the epidermal growth factor receptor (EGFR)-specific antibody cetuximab in combination with radiotherapy
- Palliative treatment
 - Chemotherapy and cetuximab or a less toxic treatment/supportive care

Prognosis

- Far more favorable outcome of HPV+ve compared with HPV–ve OPSCC
 - So substantial that the tumor-node-metastasis (TNM) staging for HNSCC was adapted to include p16INK4A immunostaining as a surrogate for HPV status
- In contrast to breast cancer, for instance, classification based on gene expression profiles is not yet common practice: on the horizon
- Prognosis is 50%; recur mostly at the locoregional site
 - Distant metastases can occur
 - Second primary sites occur in 2-3%: Notoriously difficult to treat

Effects of Treatment



<https://diseasespictures.com>



<https://medgadget.com>



What can we do?

- Screening and referral
- Research—explosive topic
- Vaccines

HPV Vaccination

Oropharyngeal Cancer (OPC) and HPV Prevention in Children
5 Key Points that Pediatricians Need to Know

1. HPV is the leading cause of OPC.
2. HPV is preventable.
3. HPV is a common virus.
4. HPV is a common virus.
5. HPV is a common virus.

Answering Questions About HPV Vaccine: A Guide for Dental Professionals

HPV is the leading cause of OPC. HPV is preventable. HPV is a common virus. HPV is a common virus. HPV is a common virus.

HPV Vaccination

- Many of these cancers **could be prevented with vaccination.**
- HPV vaccination is recommended for preteen **girls** and **boys** at age 11 or 12 years
- Immune response better in preteens
- Women → HPV vaccine until age 27
- Men → HPV vaccine until age 22 years old
 - Young men who have sex with other men or who have weakened immune systems can also get HPV vaccine until they are 27.

HPV Vaccine Doses

- 2006:
 - 3 doses over six months
- Currently:
 - Persons starting the series ages 9-14: **2 doses**
 - 2nd dose given 6-12 months after 1st dose
 - Adolescents who receive their 2 doses less than 5 months apart require a 3rd dose of HPV vaccine
 - Teens and young adults 15 through 26: **3 doses**
 - People with certain immunocompromising conditions aged 9 through 26: **3 doses**

Safety of HPV Vaccines

- All three HPV vaccines—Cervarix®, Gardasil®, and Gardasil® 9—went through years of extensive safety testing before they were licensed by FDA.
 - Cervarix® trials >30,000 females
 - Gardasil® trials >29,000 females and males
 - Gardasil® 9 trials >15,000 females and males
- No serious safety concerns identified
- CDC and FDA continue to monitor HPV vaccines to make sure they are safe and beneficial for the public.

HPV Vaccine Efficacy

- Works extremely well
 - Clinical trials: close to 100% protection against precancers and, for Gardasil and Gardasil 9, genital warts
- Significant ↓ in HPV infections since introduction in 2006
- ↓ teens and young adults with genital warts
- Australia (higher HPV vaccination coverage): ↓ precancers of the cervix in young women
- Long-lasting protection against HPV infection and HPV disease (10 years of data)
- No evidence that HPV vaccine loses protection over time

References

- CDC
 - <https://www.cdc.gov/vaccines/vpd/hpv/public/index.html>
 - <https://www.cdc.gov/hpv/parents/whatishpv.html>
- Human Papillomavirus Testing in Head and Neck Carcinomas. Guideline from the College of American Pathologists
- Leemans RC, Snijders PJF, Brakenhoff RH. Review: The molecular landscape of head and neck cancer. *Nature*. May 2018.

Types of Vaccines

- 3 licensed by the U.S. FDA
- **Gardasil:** quadrivalent HPV vaccine (4vHPV)
 - HPV types 6, 11, 16, and 18.
- **Gardasil-9:** is a nine-valent HPV vaccine (9vHPV)
 - HPV types 6, 11, 16, 18, 31, 45, 52, and 58
- **Cervarix:**
 - HPV types 16, 18
- All three HPV vaccines protect against HPV types 16 and 18 which cause most HPV cancers

HPV Vaccine Side Effects

- Minimal to None
- Most common (usually mild):
 - Pain, redness, or swelling in the arm where the shot was given
 - Fever
 - Headache or feeling tired
 - Nausea
 - Muscle or joint pain
 - Fainting
 - Rarely, allergic reactions
 - People with severe allergies to any component of a vaccine should avoid

Thank you

Questions?