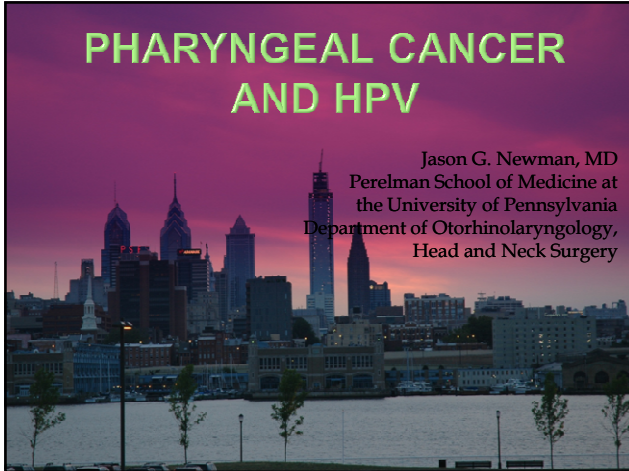



# PHARYNGEAL CANCER AND HPV

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## Disclosures

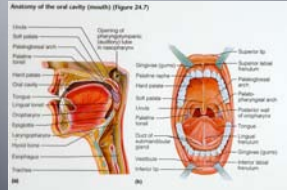
- Proctoring for Intuitive Surgical
- Medical Board, Visionsense Inc.



Otorhinolaryngology Head and Neck Surgery at Penn  
Residency in Otolaryngology, Laryngology and Head and Neck Surgery at Penn



## Anatomy



**Anatomy of the oral cavity (mouth) (Figure 24.7)**

- Boundaries:
  - Junction of the hard and soft palate superiorly
  - Hyoid inferiorly
  - Junction of the anterior 2/3 of the tongue with the base of tongue anteriorly
  - posterior pharyngeal wall posteriorly
- Includes:
  - soft palate
  - Tonsils
  - tonsil pillars
  - posterior pharyngeal wall
  - base of tongue

## The cancer burden

- American Cancer Society's estimate oral cavity & oropharyngeal cancers in the United States 2013:
  - 36,000 cases
  - 6,850 deaths
  - More than twice as common in men
  - Equally common in blacks and in whites.
  - Rate of new cases has been stable in men, dropping slightly in women.
  - Recent rise in cases of oropharyngeal cancer linked to infection with human papilloma virus (HPV) in white men and women .
  - Death rate decreasing over the last 30 years.

## This is NOT the oral cavity!



Douglas' representatives denied The Guardian's headline stating that oral sex caused the actor's cancer on Monday morning, telling USA Today, "Michael Douglas did not say cunnilingus was the cause of his cancer. It was discussed that oral sex is a suspected cause of certain oral cancers as doctor's in the article point out but he did not say it was the specific cause of his personal cancer."



### SEER Stat Fact Sheets: Oral Cavity and Pharynx

Cancer: Oral Cavity and Pharynx

It is estimated that 41,390 men and women (29,620 men and 11,760 women) will be diagnosed with and 7,890 men and women will die of cancer of the oral cavity and pharynx in 2013.

The following information is based on NCI's SEER Cancer Statistics Review. Use the links on this page to learn more about each statistic type.

## Oral Cavity vs. Oropharynx

- Role of smoking and drinking
- Role of HPV
- Symptoms
- Rate of new cancer diagnoses
- Treatment algorithms
- Rate of cure



*Oral and Head/Neck Cancers at Penn State: A Review of the Literature, Etiology and Research from 1970*



## What's the role of HPV

- Double stranded DNA virus
- Several hundred subtypes
- Unique to humans
- Type 16 and 18 are known carcinogens, but other less common ones (31,45) are also carcinogens
- Infects the basal epithelial cells
- Replicates with the host genome

## HPV mechanism

- At cellular level, similar to changes seen in cervical cancer
- E6 and E7 "early" genes
  - p-53 and pRB/p-16
- Distinct changes compared to non-HPV oropharynx cancers

## Mechanisms of action

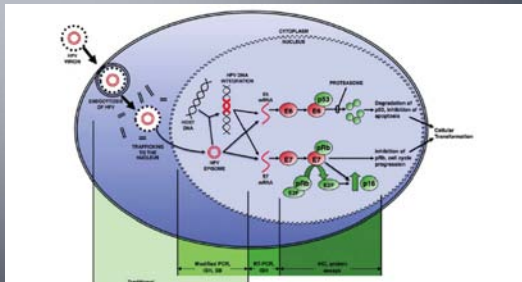


Fig. 1. Schematic of HPV infection of a mucosal cell. After virus entry via endocytosis, the virus establishes a persistent infection as a viral episome or integrates into the host genome. HPV E6 and E7 oncoproteins are expressed from both forms of the viral DNA, which lead to p53 degradation and its inhibition, respectively. Methods of HPV oncoprotein or p16 detection are depicted with respect to stage of HPV biologic activity.

## The role of HPV

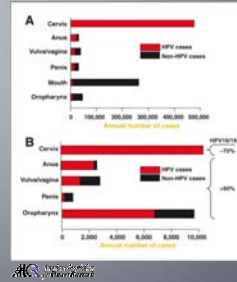


Figure 1. A, worldwide incidence and distribution of HPV-associated cancers. Red, HPV-positive cancer; white, HPV-negative cancer. B, incidence and distribution of HPV-associated cancers in the United States (data from refs. 3 and 4). The approximate percentage of HPV-associated cancer attributable to HPV16 and -18 is also shown. Red, HPV-positive cancer; white, HPV-negative cancer.

## Increasing HPV burden in cancer

- ❑ Burden of HPV oropharynx cancer is approaching (maybe passing) the burden of cervical cancer in the US.
- ❑ Total number of non-cervical cancers caused by HPV in the US is higher than the total number of cervical cancers
- ❑ We have no screening
- ❑ The incidence continues to rise



Division of Infectious Diseases and Global Health, Penn  
 Research in Tobacco, Cancers, Infections and Research since 1970



## What do we do?

- ❑ We have a vaccine! (or two)
  - Gardasil- HPV 6, 11, 16, 18
  - Cervarix- HPV 16,18
- ❑ Over 95% effective at preventing pre-cancers and cancers (cervical and vaginal) caused by HPV
- ❑ Not effective if patient already infected
- ❑ No proof yet, but preliminary research suggests it will be effective against oropharynx cancer

## Need to improve public awareness

- This is a cancer vaccine not just an STD vaccine!
  - AAP and CDC- noted vaccine curves have flattened
- Vaccinate boys and girls
  - Higher incidence of this cancer in men
- According to the CDC, estimated 26,200 HPV related cancers in 2010
  - 17,400 in women (10,300 cervical)
  - 8,800 in men (6700 oropharynx)
  - Rates of HPV related cancer going up (compare to oral cancer)

## In the meantime

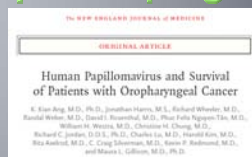
- Forced to reconsider some of our most routine “truths” in head and neck cancer
  - Patient demographics
  - Risk factors
  - Results of previous studies (race, gender, new drugs or surgeries, different demographics or countries)
  - Role of staging, nodes
  - Role of ECS



*Observational Study of Head and Neck Cancer at NCI  
Survival in Patients with Unknown and Known Oral HPV*



## Improved prognosis



- RTOG 0129
  - Accelerated fraction RT and platinum compared to standard RT with platinum
  - Controlled for HPV
  - Survival (regardless of arm) was significantly different in HPV+ (82 vs. 57%)

## HPV and Management of OP Cancer

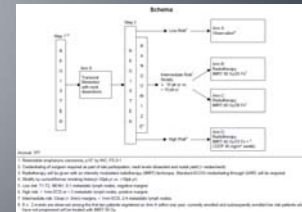
- Studies imply we should intensify treatment for HPV negative patients, and de-intensify for HPV positive
- NCCN currently has no recommendations for how to do this
- Several upcoming studies

### HPV Stratification Studies: Non-Surgical

- ☐ ECOG 1308
  - HPV + patients
  - Induction chemo with deintensification of RT for CR
- ☐ RTOG 1016
  - HPV + patients
  - Platinum based CRT vs RT with cetuximab

### HPV Stratification Studies: Surgical

- ☐ ECOG 3311
  - HPV + patients
  - Randomized Phase II Trial
  - Transoral surgery then randomize intermediate group to standard vs de-intensified RT
- ☐ RTOG 1221
  - HPV - patients
  - Randomized Phase II Trial
  - Transoral Endoscopic Head And Neck Surgery followed by Risk-Based IMRT and Weekly Cisplatin versus IMRT and weekly Cisplatin



ECOG 3311 Schema

### Treatment options

- ☐ Primary radiation
- ☐ Primary Surgery
  - Open
  - Laser
  - Robotic

### Counseling patients

- ☐ Increased risk of oral HPV infection with:
  - Increasing number of lifetime oral or genital sexual partners
  - Increased number of recent sexual partners and open mouth kissing
  - Participation in "casual" sex
  - History of STD



Division of Otolaryngology, Head and Neck Surgery at NIDDK  
Research in Tobacco, Cervix, Oropharynx and Oesophagus areas 10/13



## Counseling patients

- ❑ 85-90% of humans will be infected with the HPV virus
- ❑ Most people clear it within 1-2 years of infection
- ❑ Virus, like many viruses, can remain dormant and then resurface

## Conclusion

- ❑ HPV testing should be considered a reflex test
  - All head and neck SCCa
  - All head and neck unknown primary
- ❑ Counsel patients
- ❑ Counsel doctors and media
- ❑ Participate in clinical trials

Thanks!

