

# Management of HPV-Related Head and Neck Cancer



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# Highlights



- Epidemiology
- Tumorigenesis
- Typical Patient
- Prognosis
- New Staging
- Treatment paradigms
- Vaccine

# Epidemiology

## Exposure to HPV very common

- Point prevalence 43-62%;
- Transmitted sexually, skin to skin
- Infections are asymptomatic
  - Vast majority clear the infection;
  - Only half will develop antibodies to HPV
- 7% population has a prevalent OP HPV infection
  - 65-100% sexually active adults have been exposed

# Epidemiology

Lifetime prevalence of OP infection is higher

- Most will Clear the infection and never develop cancer
- Seropositivity not an accurate reflection of prior HPV infection

Odds ratio 3:1

- >8-10 sexual partners
- >6 oral sex partners

# Epidemiology

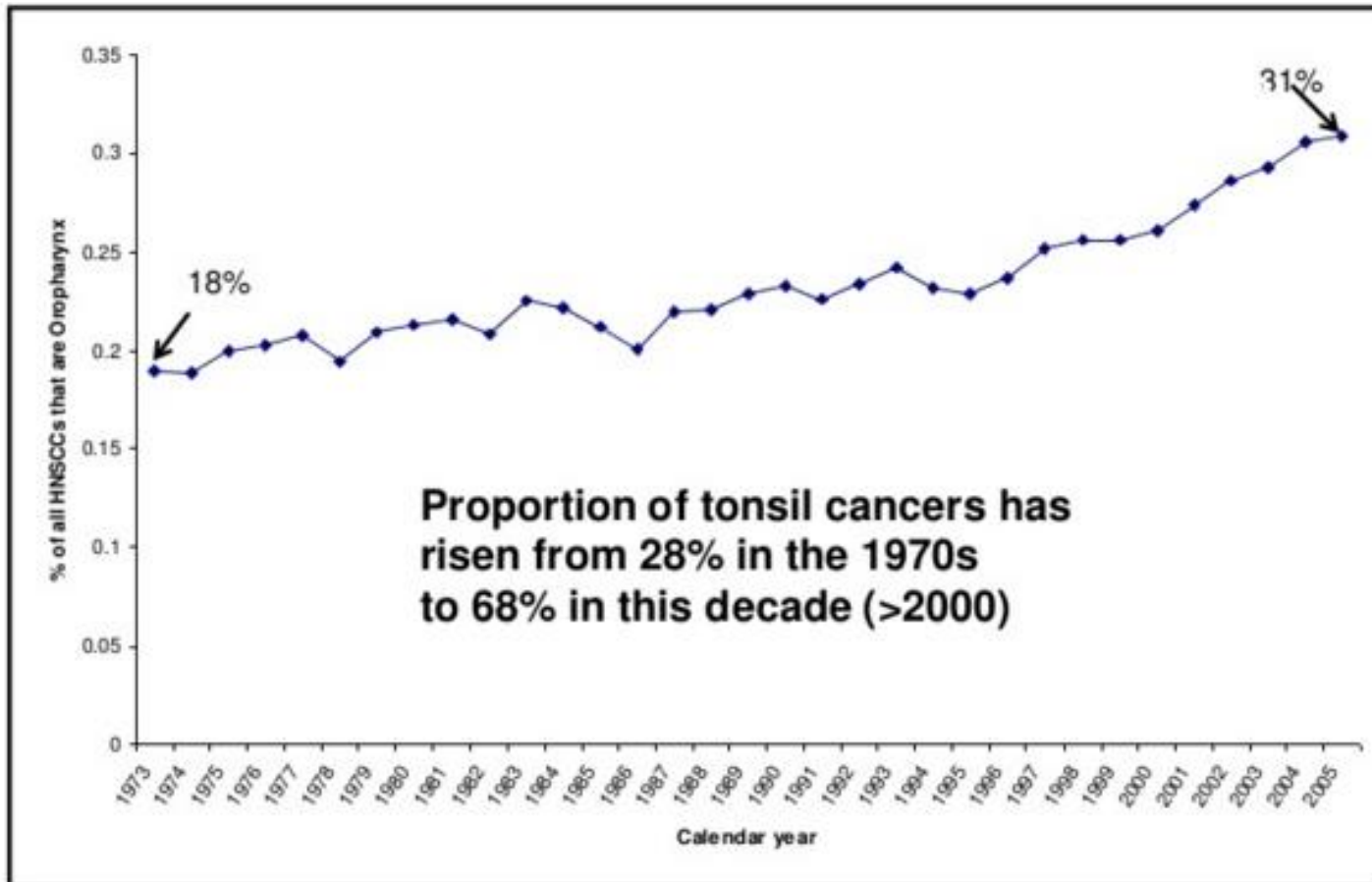
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- Incidence of oral HPV increases with number of oral sexual partners

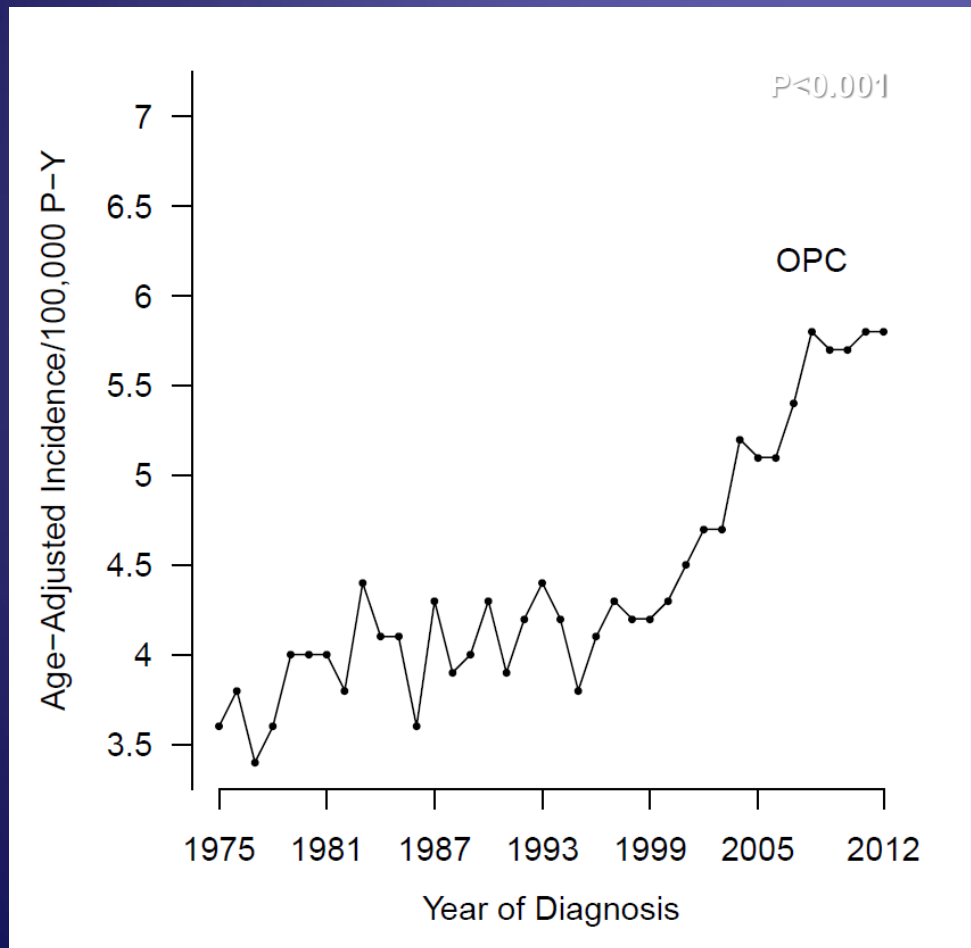
\*This is an *epidemic*; we will not see the peak until approx 2030

HPV infection likely precedes development of cancer by years if not decades

# Incidence



# Incidence of OPC in the US: SEER (1975-2012)

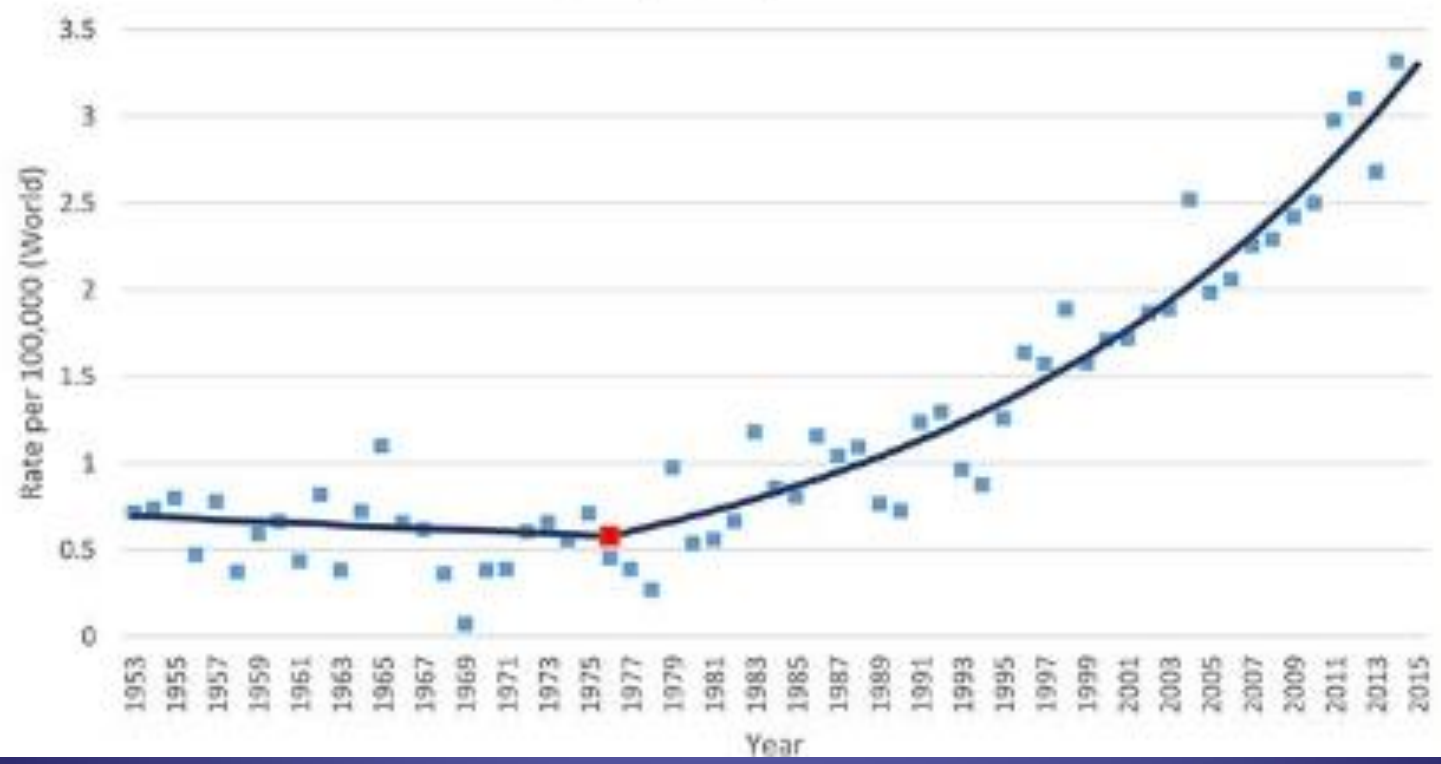


Patel et al. Cancer 2016

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

C

### Oropharynx SCC



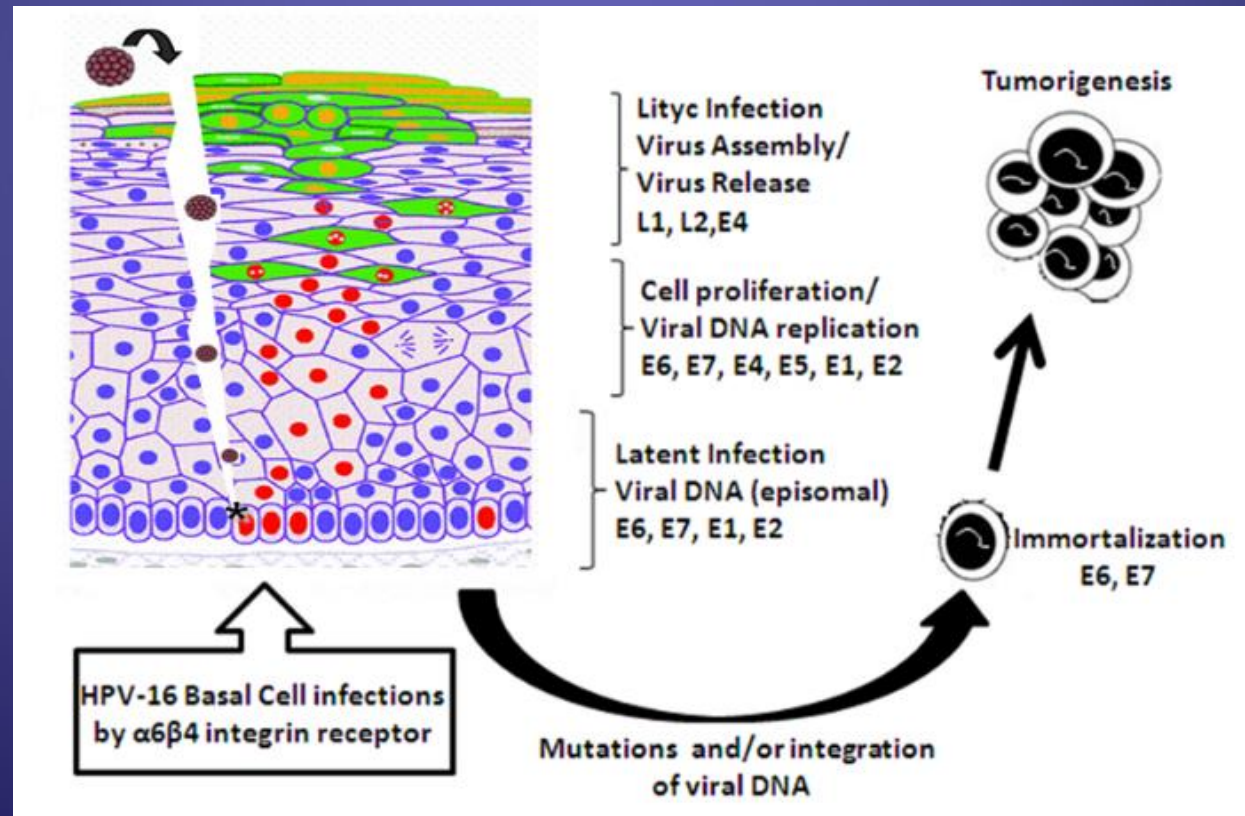


# HPV Virology

- 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

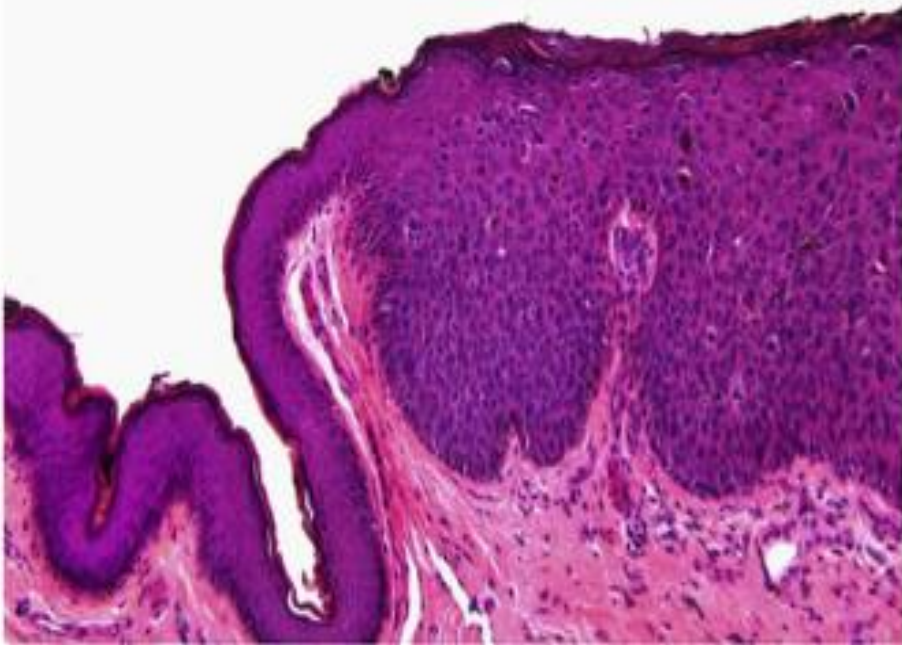
# Tumorigenesis

HPV viral DNA integrates into human keratinocyte; oncogenic proteins E6 and E7 expressed >binds to p53>Unchecked cell division

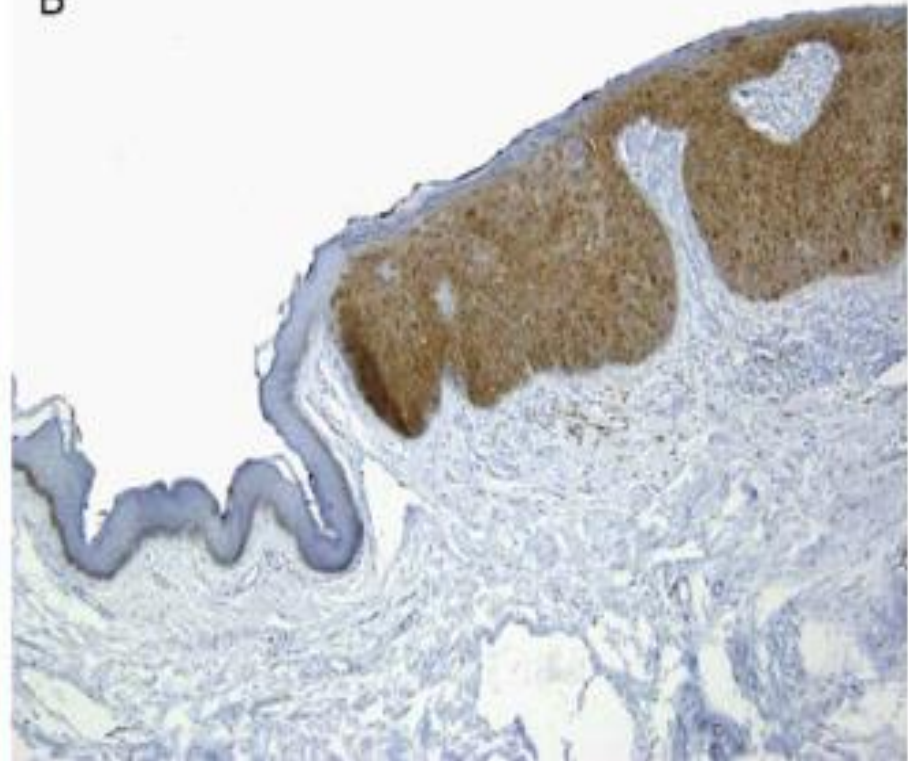


# HPV Epidemic

A

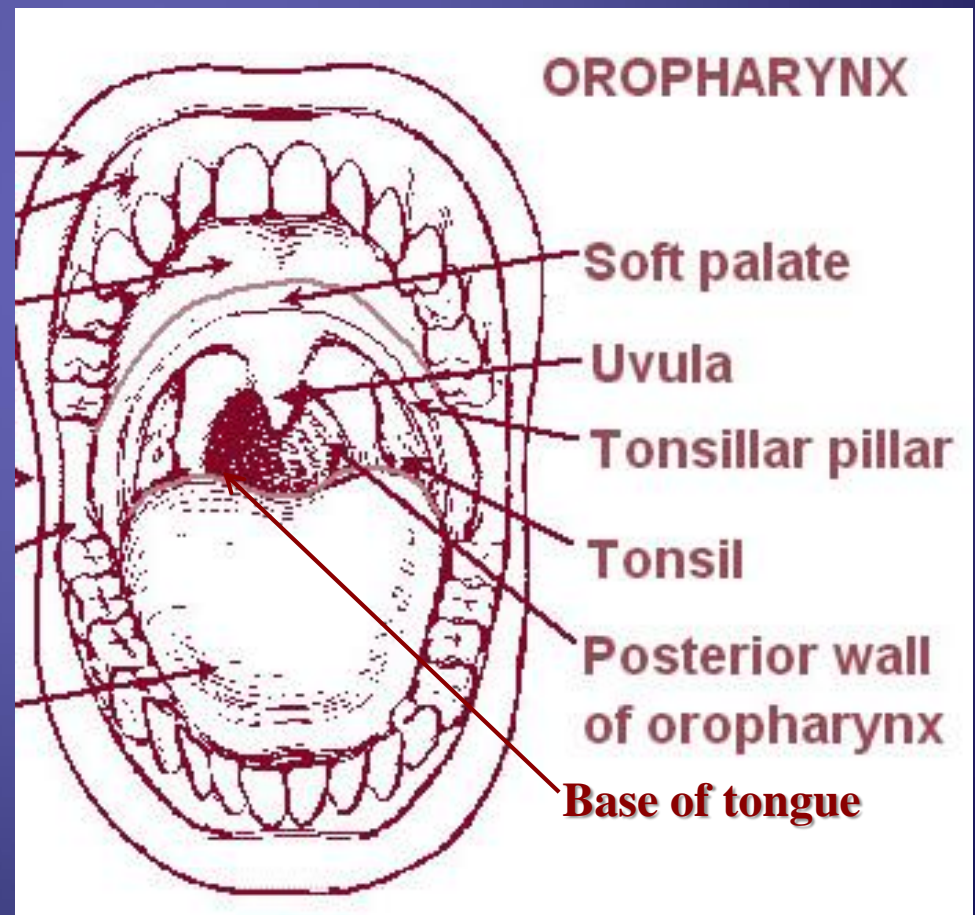
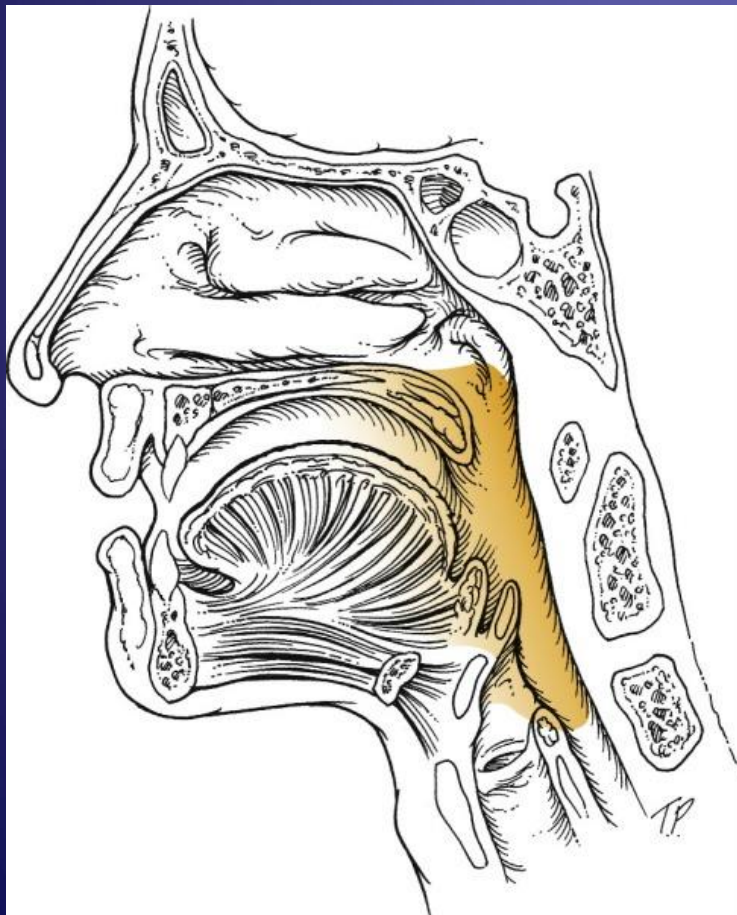


B



# Where does HPV + OPC occur?

Palatine tonsils and base of tongue

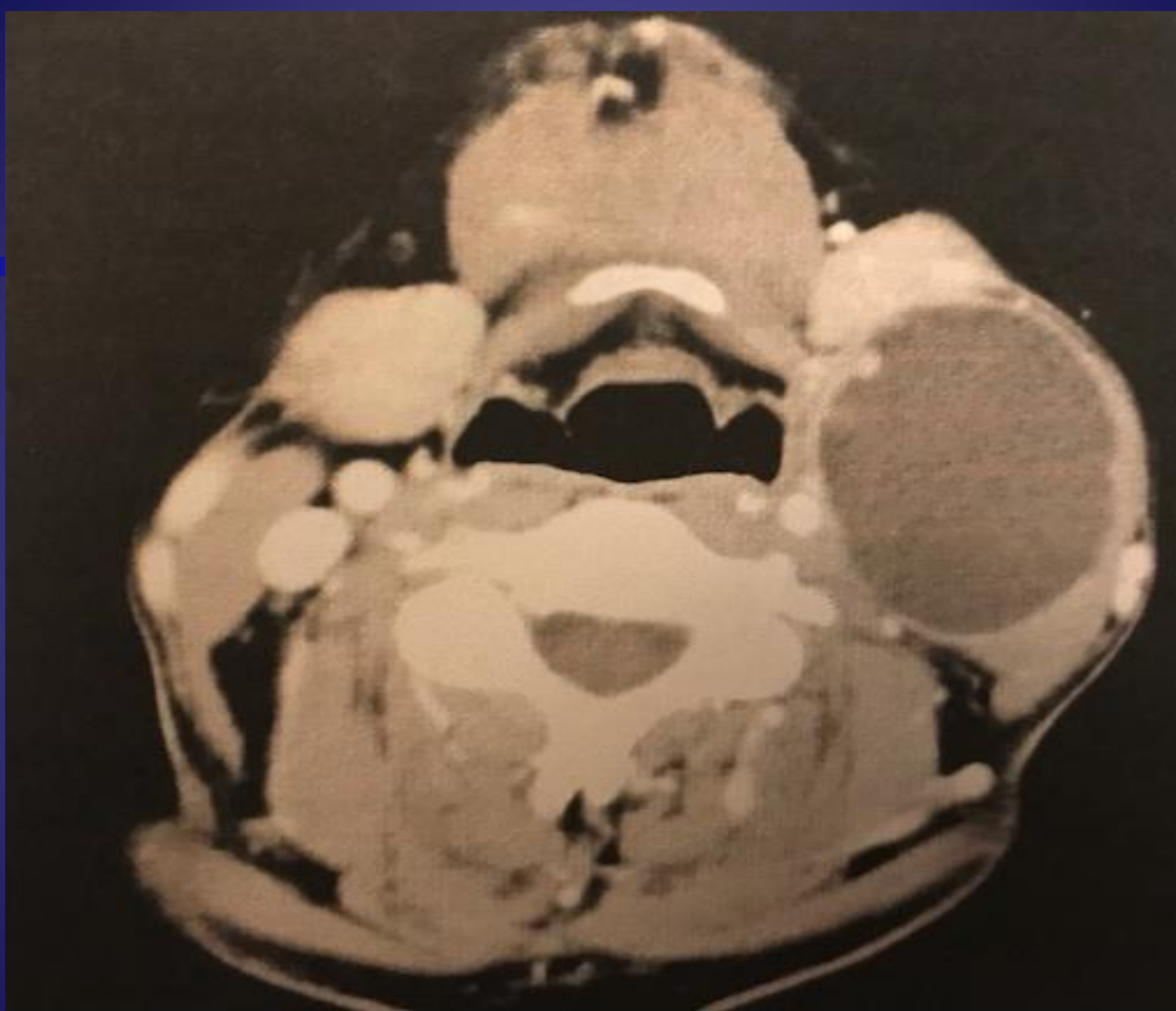


# Presentation

- Cystic lymph nodes
- basal layer of tonsillar crypt is infected, arises in deeper areas of tonsil/lymphoid crypts; not on the surface
- 90% of all Carcinoma Unknown Primary (CUP) are HPV+

*most are found with tonsillectomy and BOT resection (TORS)*





# Oropharyngeal cancer: management

**Non surgical**

**Radiation**

**Chemoradiation**

**Surgical**

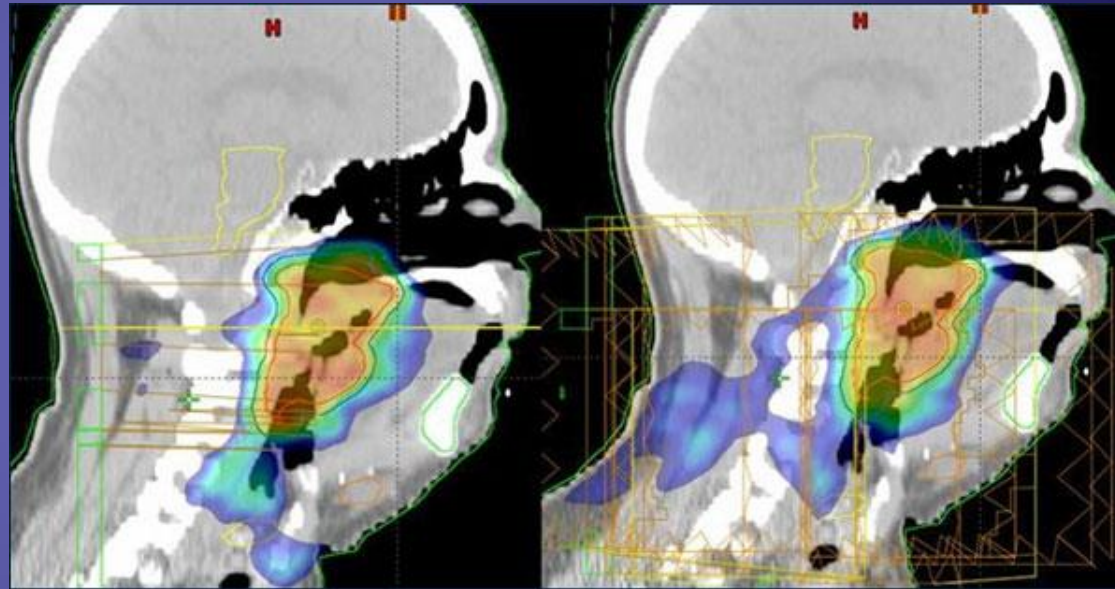
**Open**

**Transoral**

**-Standard**

**-Robotic resection**

**-Laser resection**





# Prognosis

- Dramatic improvement of 5YS through unclear mechanism; platform independent
- Smoking affects prognosis
- Better rx to chemo, CRT

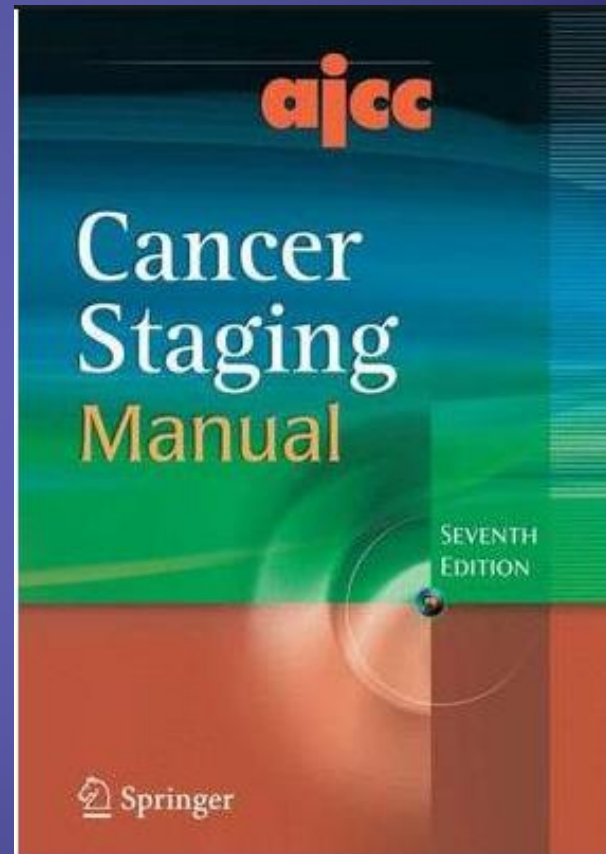
*Patient's with HPV positive status have about an 86% reduction in the risk of recurrence compared with patient's with HPV negative cancer*

# Prognosis

- Extracapsular extension, not a negative risk factor in HPV+
- Chemotherapy does not improve survival when added to PORT; may increase incidence of Gtube dependence
  - (JAMA Otolaryngol March 2017 Wash U)
- Some evidence for risk for distant relapse for up to 5 years
- Better survival persists even after progression

# Staging

- 7th Ed staging Manual  
TNM for HPV-OPC  
not appropriate
  - \*Had little prognostic  
value for HPV patients
  - \*AJCC was established  
before HPV-driven OPC  
was recognized as a  
distinct entity



# “Sobering Reality”

Brizel (JCO March 2015)

“...Just as investigators were developing more aggressive therapies, the disease itself was changing...”



# New Staging

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AJCC 8<sup>th</sup> Edition; January 2018

ICON-S: Intl Collaboration on OPC Network  
for Staging

- Superior stratification of overall and progression-free survival (*Cancer* May 2017)

# New Staging

**TABLE 6. Anatomic Stage and Prognostic Groups for *Clinical* TNM Grouping of Human Papillomavirus-Associated (p16-Positive) Oropharyngeal Cancer, 8th Edition Staging Manual<sup>a</sup>**

T CATEGORY	N CATEGORY			
	N0	N1	N2	N3
T0	NA	I	II	III
T1	I	I	II	III
T2	I	I	II	III
T3	II	II	II	III
T4	III	III	III	III

<sup>a</sup>Any M1 is stage IV.

# Treatment

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Why de-intensify??

- The HPV+ typical patient population is living long enough to experience the long-term side effects of chemoradiation
- (tooth loss, ORN, dysphagia, muscle spasms)

**New endpoint:**

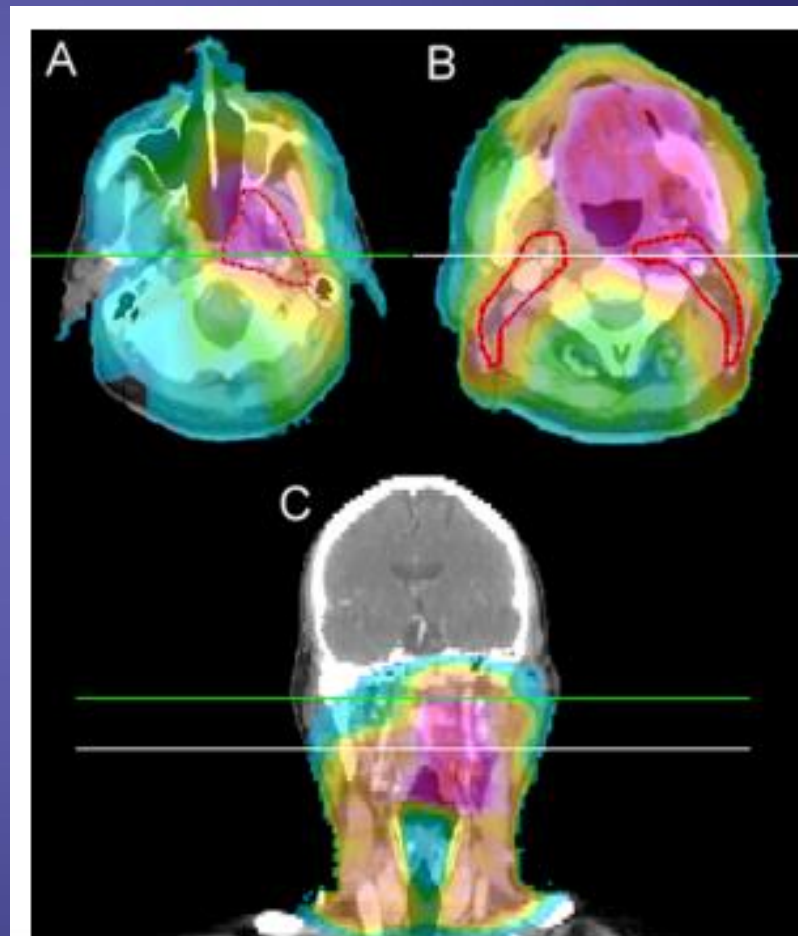
**Toxicity-free survival**

# Treatment

- Radiation

Eliminating contralateral and retropharyngeal nodes has minimal risk of failure

*Cancer* 2014; 488 pts; no out-of-field recurrences





# Treatment Paradigm

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## **Surgery** (must be functional)

- Provides critical pathologic information, can alter stage; post-op RT is strategic;
- Does not compromise survival

## **With Strategic deintensified PORT**

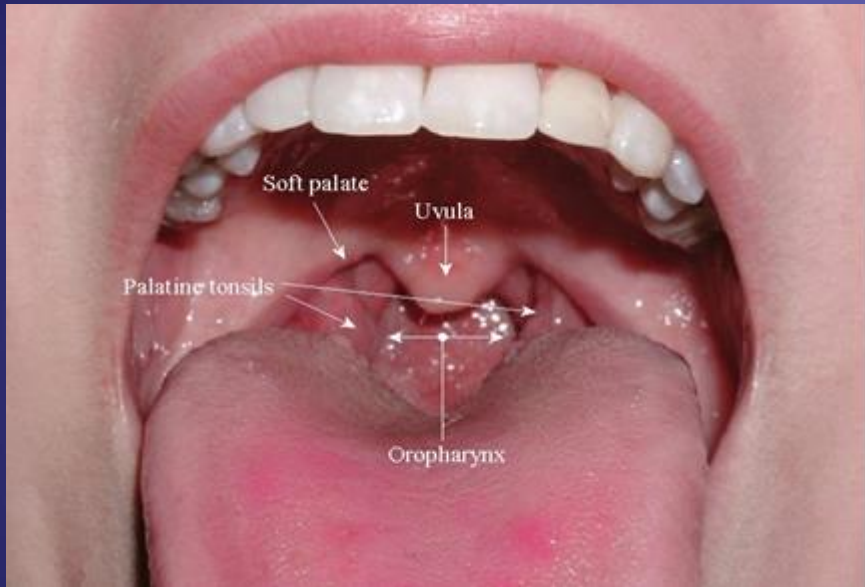
Every 1000cGy imparts a 19% increase chance of severe dysphagia

# Treatment

Transoral surgery +/- PORT same survival  
with better function than CRT

*Head and Neck 2016; 153 patients*





# Patient Examples

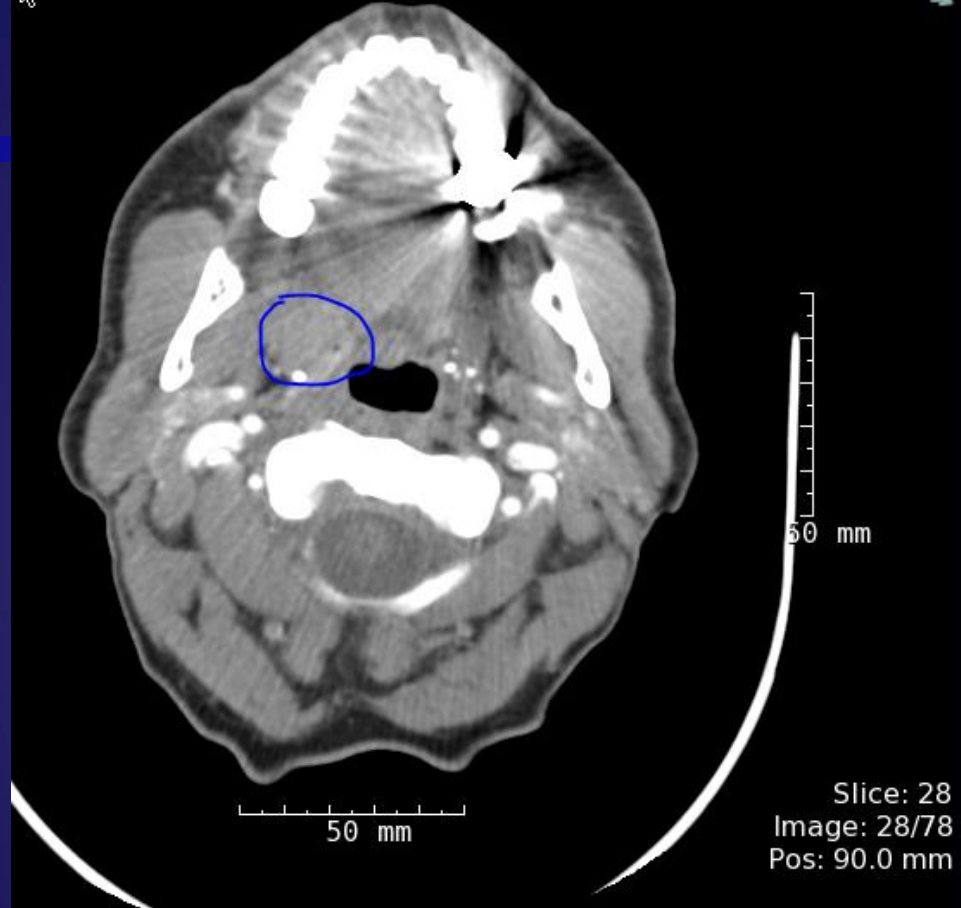
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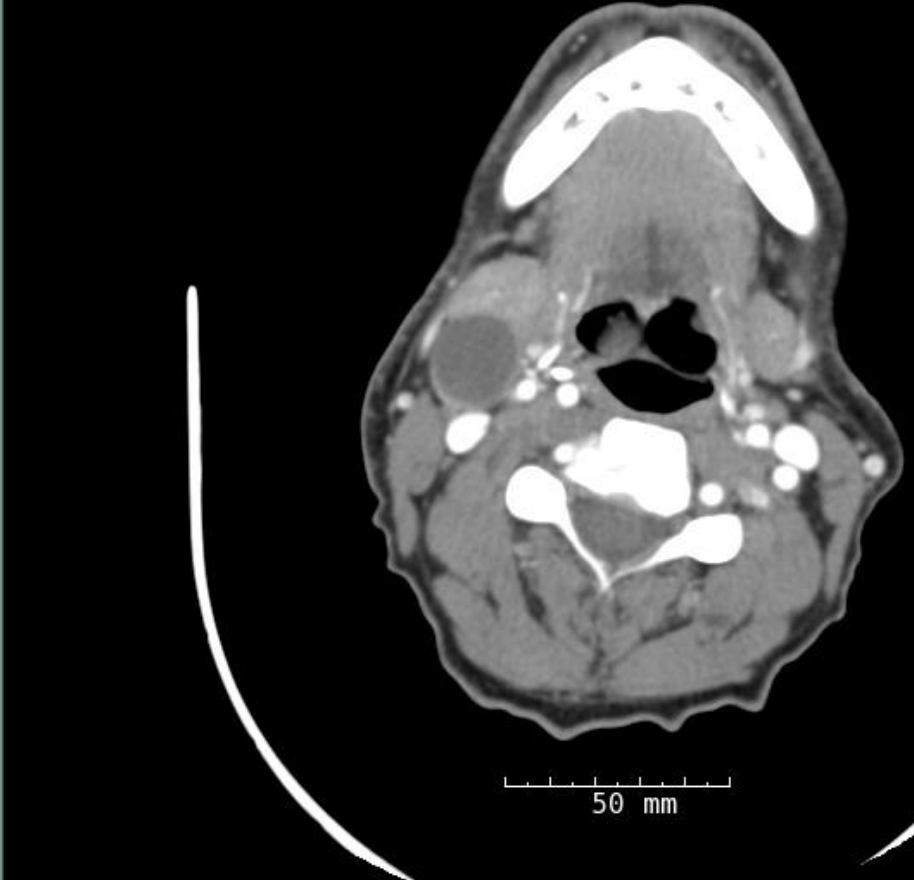
# Case presentation

- 50 year old man notices a lump while shaving. No other symptoms; feels great (golfs, runs, full time job, kids etc). Non-smoker. Maybe recent URI
- PCP gives 2 rounds of antibiotics
  - After antibiotics obtains CT scan which shows enlarged lymph node
- Neck mass in adult needs evaluation!

SSUE NECK WITH IV CONTRAST/S.T. NECK (-)



Series: CT SOFT TISSUE NECK WITH IV CONTRAST/S.T. NECK (-)  
Date: 3/2/17





# Vaccine

- Gardasil 9: nonavalent HPV6, 11, 16, 18, 31, 33, 45, 52, and 58

Vaccine has decreased prevalence of oral HPV infection with 93.3% efficiency

- No visible pre-malignant lesion screening exam not possible

Due to long latent period before cancer development in OPC, direct study to prove efficacy in preventing OPC is unlikely

get your kids vaccinated!





# Goals of vaccination

- Shown to effectively prevent anogenital HPV infection, premalignancy and cancer
- Impart immunity to strains of HPV prior to exposure
  - Decrease burden of infection/exposure/ HPV-related cancer on a population level



# Barriers to vaccination

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- Limited understanding
- Unaware of additional doses
- Safety concerns
- Discomfort re: sexual behavior
  - Parental belief that child is too young
- Limited clinician time, reimbursement
- **Success dependent on health care professionals!**
  - Education is critical

# Can I get cancer from oral sex?

Yes, and the U.S. is seeing a sharp increase in the number of cases of oral and throat cancer especially among young men, caused by HPV infections contracted during oral sex.

Tuesday, September 20, 201

D2 •

REPORT ON HEALTH

## The Rising Risk: HPV now a more-common cause of throat and oral cancers than tobacco

Changing sexual behavior may explain why over the last decade HPV infections have led to a **four- to five-fold increase** in the number of tonsillar and base of tongue cancers, particularly among young men.

Survival rates for mouth and oral cancers are **between 85%-90%**, but oral cancers alone still **kill 8,000 people** in the U.S. every year.

In 2010, the National Cancer Institute estimated there were 12,660 cases of oropharyngeal cancer resulting in **2,410 deaths**. About half of those cases were men and **at least 75% were caused by HPV**.



HPV is a virus. It is the most common sexually transmitted infection, and can be spread through skin-to-skin contact.



Approved vaccines can help prevent an HPV infection.

# Oral HPV transmission

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- Oral HPV is not casually transmitted (i.e., by sharing drinks, kiss on the cheek)
- Partners have likely already shared any infections
- With new partners, discuss protection methods (e.g., condoms, barrier protection)
- Exposure does not mean cancer

Annals of  
Oncology 28:  
3065–3069, 2017  
doi:10.1093/annonc/mdx535  
Published online  
19 October 2017



# Partner's level of risk...

- Rate of oral HPV infection among partners is same as that among general population (no increased risk)
- Partners of patients with HPV-associated HNSCC *may* have slightly higher rates of HPV-associated cancers (anal, penile, oropharyngeal) but these cancers remain rare
- Chances of developing these cancers remain low overall

# Patient Communication

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- AHNS.info web site
- How did I get HPV?
- Am I contagious?
- Should I get the vaccine?
- Will the virus die when my cancer is cured?

Be inclusive, honest and positive!

Thank You!



Questions?