

WINTER REFRESHER COURSE FOR FAMILY MEDICINE


HPV-RELATED HEAD AND NECK CANCER

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DISCLOSURES






TAKE HOME POINTS

- The incidence of HPV-related oropharyngeal cancer has continued to rise
- It affects younger, healthier males
- The treatment of HPV-related oropharyngeal cancer continues to evolve
- Late effects of treatment can be devastating
- There is a presumption of immunization benefit


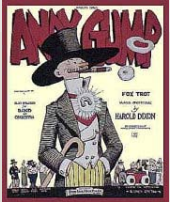
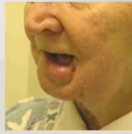




TRADITIONAL PRESENTATION OF HEAD AND NECK CANCERS


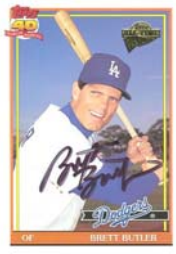


- Smoker-Drinker older male
- Painful mass, ulcer, nodule
- Change in longstanding leukoplakia
- Articulation change
- Otalgia
- Bleeding
- Weight loss
- Dysphagia
- Airway obstruction with stridor
- Hoarseness
- Neck mass

MANDIBULAR DEFECTS

OROPHARYNX CANCER PATIENTS

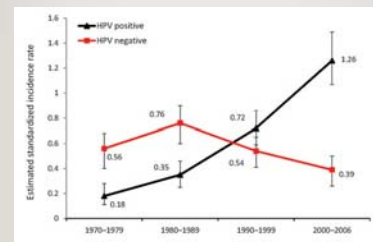
CANCERS WITH RISING INCIDENCE 1999-2008

- Pancreas
- Liver
- Thyroid
- Kidney
- Melanoma
- Esophageal adenocarcinoma
- HPV-positive oropharynx

Simard, *Ca: Cancer J Clinicians* (published online: 4 JAN 2012)



Trends in HPV-Positive and HPV-Negative Oropharyngeal Cancers per 100,000



<https://wwwnc.cdc.gov/eid/article/16/11/10-0452-f3>



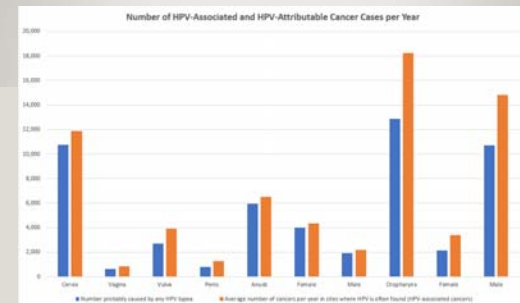
WISCONSIN OROPHARYNX CANCER INCIDENCE CASES PER 100,000 1995-2011



Source: Wisconsin Cancer Reporting System, Office of Health Information
Division of Public Health, Department of Health Services, 2014



HPV DETECTION BY SITE



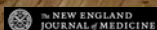
Saraiya M, et al, US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. *J Natl Cancer Inst.* 2015 Jun; 107(6):djv086. Published online 2015 Apr 29. doi: 10.1093/jnci/djv086



ASSOCIATION BETWEEN ORAL HPV INFECTION AND OROPHARYNGEAL CANCER

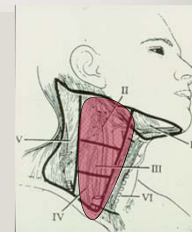
- OP cancer significantly associated with
 - Oral HPV-16 infection (OR 14.6)
 - Seropositivity for the HPV-16 L1 capsid protein (OR 32.2)
 - Oral infection with any of 37 types of HPV (OR 12.3)
- Sexual activity associated with OP cancer
 - >25 vaginal partners (OR 3.1)
 - >5 oral sex partners (OR 3.4)

D'Souza *NEJM* 2007 356:1944-1956



NATURAL HISTORY OF OROPHARYNGEAL CANCER

- Local invasion
- Regional metastases develop early
 - Bilateral
 - Levels II, III, IV, V



CLINICAL PRESENTATION: OROPHARYNX CANCER

60 year-old competitive athlete

- Mild sore throat with enlarged tonsil. Small bilateral lymph nodes. Throat culture negative. Two courses of antibiotics. No resolution.
- Dental evaluation negative.



MANAGEMENT OF HPV-POSITIVE OROPHARYNGEAL CANCER

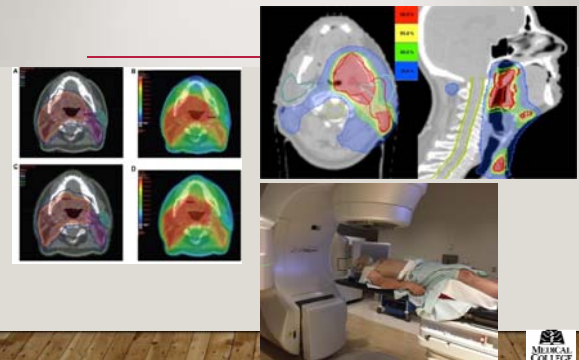
- Concurrent Platinum-based chemotherapy and radiation therapy
- Concurrent cetuximab and radiation therapy
- Surgery with postoperative radiation therapy
 - Transoral laser microsurgery (TLM)
 - Transoral Robotic Surgery (TORS)



SURGICAL APPROACHES



RADIATION APPROACHES

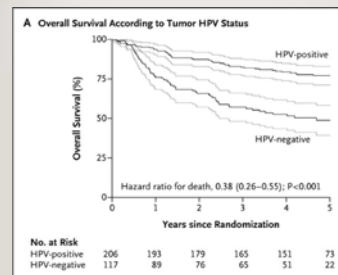


CHEMOTHERAPY AND IMMUNOTHERAPY APPROACHES

- Concurrent
- Neoadjuvant
- Cisplatin-based
- Cetuximab-based
- De-escalation trials
- Immune checkpoint inhibitors for recurrent cancer (pembrolizumab and nivolumab)
- Clinical trials (31 currently recruiting)



Overall Survival Based on Tumor HPV Status



Ang, *N Engl J Med* 2010; 363:24-35

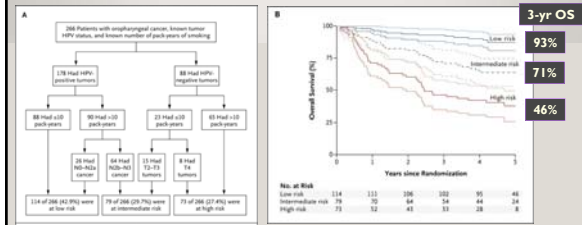


AJCC 8TH EDITION – OROPHARYNX CANCER

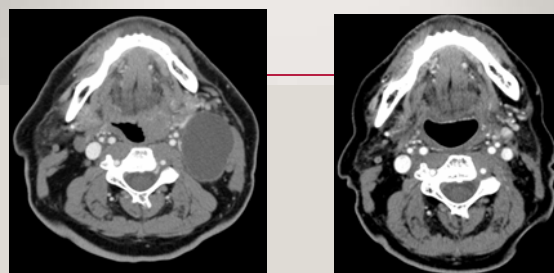
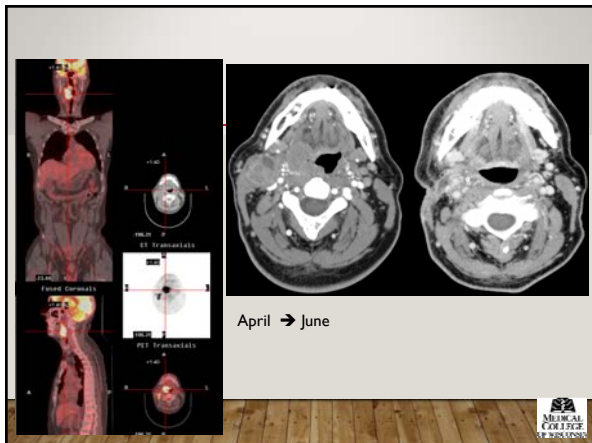
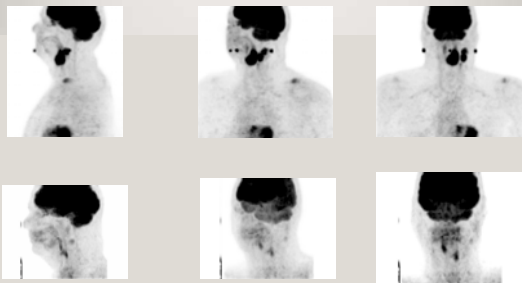
AJCC Comprehensive Stage	T and N staging	
	HPV-related (p16+)	Non HPV-related
Stage I	T0-T2N0-N1	T1N0
Stage II	T0-T2N2 or T3N0-N2	T2N0
Stage III	T4 or N3	T1-3N1 or T3N0
Stage IVA	M1	T1-T3N2a-N2b or T4aN0-N2b
Stage IVB	NA	Either T4b or N2c
Stage IVC	NA	M1



Risk Stratification Based on HPV, Smoking, Tumor Size, and Nodal Size



PET Scan: Tumor Response April to October



THREE-YEAR FOLLOW-UP

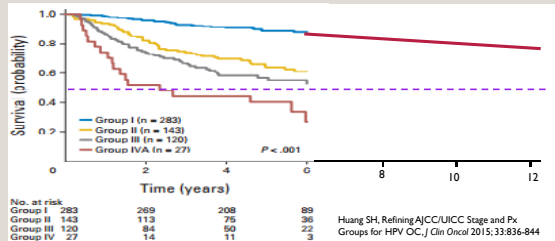


ETIOLOGIES AND ASSOCIATIONS – 2019

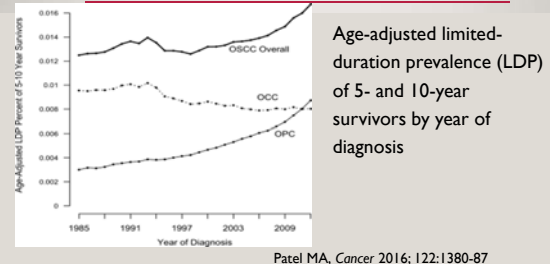
- Tobacco
- Alcohol
- Human Papilloma Virus (especially HPV-16 and 18)
- Genetics
- Diet (Vitamin A, C, E)
- Dental irritation; poor oral hygiene



EXPECT MORE LONG-TERM SURVIVORS

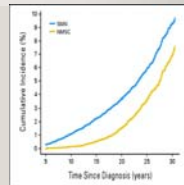


EXPECT MORE OROPHARYNGEAL SURVIVORS



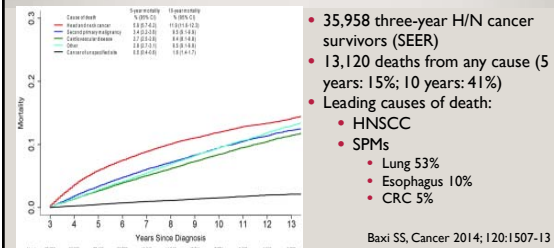
EXPECT MORE SECOND MALIGNANCIES

- Childhood Cancer Survivors Study (CCSS)
- 14,358 individuals
 - 802 Second Malignant Neoplasms (SMNs)
 - 66 meningiomas
 - 1007 NMSC
 - 2.3-fold increase over seven year period
 - 30-year cumulative risk:
 - SMNs – 9.3%
 - NMSC – 6.9%
 - Highest risk groups: Female, Hodgkin's or Sarcoma, Radiation



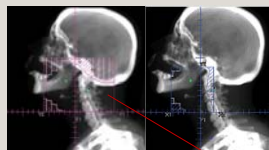
Meadows AT, J Clin Oncol 2009; 27:2356-2362

EXPECT CONTINUING CANCER DEATHS



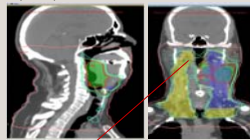
EXPECT DIFFERENCES IN RADIATION LATE EFFECTS

Three-field technique



50 Gy @ 2 Gy/Fx

Intensity Modulated Radiation Therapy (IMRT)



50 Gy @ 1.4 Gy/Fx

Shang Q, Applied Rad Onc (9) 2015

EXPECTING SHIFTING CANCER TREATMENT EFFECTS

- Different late effect profiles between chemotherapy, EGFR agents, checkpoint inhibitors
- Financial toxicity
- Persistent HRQoL Effects
- Psychosocial support requirements

Rettig EM, Cancer 2016; 122:1861-70
Holland JC, Cancer 2005; 104 (Suppl 11): 2624-37

CASE REPORT: OROPHARYNX CANCER

60 year-old competitive athlete

2004: T2 N2c M0 oropharynx cancer treated with IMRT (70 Gy in 35 Fx) with weekly carboplatin and paclitaxel, then staged bilateral MNDs

2009: Dental deterioration, fibrosis, dyspnea on extreme exertion, mild dysphagia, vocal fold hypomobility

2011: Worsening fibrosis

2015: Increased mandibular swelling, ORN treated with HBO

2016: Spontaneous mandible fracture

- Biopsy: Osteosarcoma
- Doxorubicin and carboplatin x 2 cycles
- Hemimandibulectomy and fibula reconstruction



CDC ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

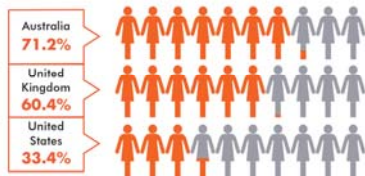
Recommended 9-valent HPV vaccine from ages 11 and 12 (can be given as young as 9) through age 45

Diseases associated with HPV

- **Oncogenic (high risk) types** – e.g. HPV 16, 18
 - Cervix cancers
 - Vagina cancers
 - Vulva cancers
 - Penis cancers
 - Anus cancers
 - Oropharynx cancers
 - High grade intraepithelial neoplasias
- **Non-oncogenic types** – e.g. HPV 6, 11
 - Anogenital warts
 - Recurrent respiratory papillomatosis



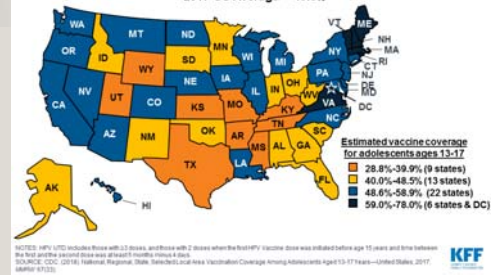
Figure. HPV vaccine 3-dose coverage among girls in high-income countries?



Source: CDC. Human Papillomavirus (HPV). For Clinicians. HPV: You Are the Key to Cancer Prevention. Page last updated September 30, 2015. cdc.gov/hpv/hcp/index.html



Figure 4
HPV Vaccination Rates of Adolescents, by State
Adolescents ages 13-17 with HPV Up-To-Date (UTD) Vaccination Series, 2017
2017 US Average = 48.6%



NOTE: HPV UTD includes those with 1-2 doses, and those with 2 doses when the first HPV vaccine dose was initiated before age 15 years and time between the first and second dose was at least 6 months minus 6 days.

SOURCE: CDC. (2016). National Regional, State, Territory, and Area Vaccination Coverage Among Adolescents Aged 13-17 Years—United States, 2017. MMWR 67(32).



TAKE HOME POINTS

HPV-RELATED HEAD AND NECK SCC OF THE OROPHARYNX

- Increasing in prevalence
- Often presents in men in their 50's and 60's
- Often presents with neck disease
- Associated with increased exposure to oral sex and increased number of partners
- MUCH better outcomes than non-HPV cancers
- Treatment options are evolving
- Encourage HPV immunization: "The Cancer Vaccine"



DO YOU RECOMMEND E-CIGARETTES? OR NOT?

Positives:

- Harm reduction
- Decreased combustible tobacco (98% of tobacco deaths)

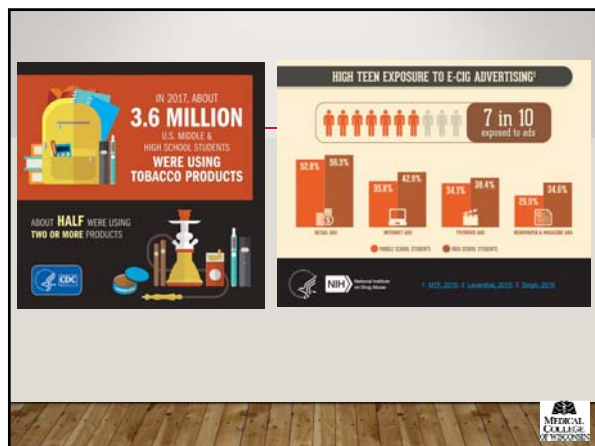
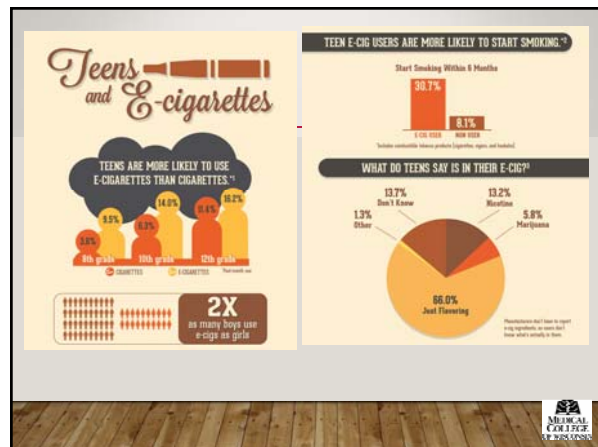
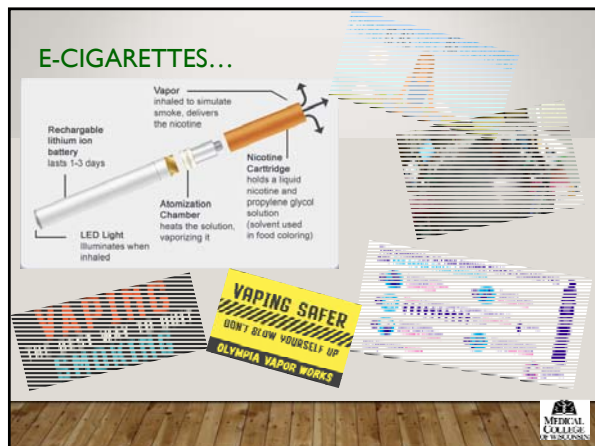
Negatives:

- Dual use
- Has not been shown to help people quit
- Aerosol (not "vapor") contains nicotine, ultrafine particles, Benzene, Cadmium, Formaldehyde, Lead, Nickel, and Toluene



Fiore MJ. *New Engl J Med* (Jan 23) 2014; 370:297-299
Goniewicz ML. *Toxicol Control* March 6, 2013
Williams M. *PLoS ONE* 8(3); March 20, 2013



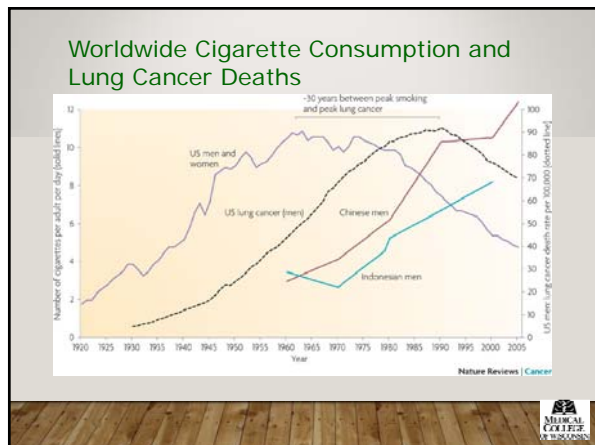




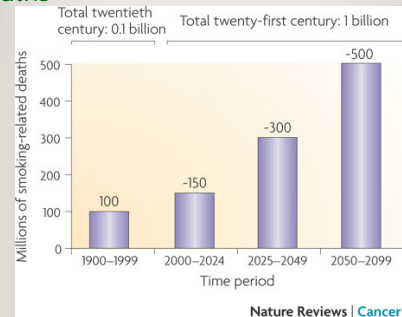
GLOBAL IMPACT OF TOBACCO

- 1.1 billion smokers worldwide
- 80% of smokers live in low- and middle-income countries (49% of men, 8% of women)
- 60% of smokers live in 10 countries (China, India, Indonesia, Russian Federation, US, Japan, Brazil, Bangladesh, Germany, Turkey)

Jha P. *Nature Reviews/Cancer* 2009; 9:655-664



Worldwide Projected Smoking-Related Deaths



COMMENTS OR QUESTIONS



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Blog: Reflections in a Head Mirror
www.Froedtert.com/reflections