Surveillance of Cancers of the Oral Cavity & Pharynx and Role of Human Papillomavirus (HPV) in Cancers of the Oropharynx

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Objectives
• Provide Overview of Oral Cavity & Pharynx Cancers, 2013
• Review Anatomy of Sites for Cancers of Region
• Describe Tools/Websites for National and State Surveillance - Cancers Oral Cavity and Pharynx
• Examine Epidemiologic Trends in Oral Cavity & Pharynx and Oropharynx Cancers
• Describe the Role of Human Papillomavirus (HPV) in Cancers of the Oropharynx Region
• Describe Public Health Implications of Current Status of Oropharyngeal Cancers

Oral Cavity and Pharynx Cancers, 2013
• Approx 264,000 persons living with these cancers
• 41,380 new cases of Oral Cavity and Pharynx Cancers
  – 29,620 men (71%) 11,670 women
• 7,800 deaths from Oral Cavity and Pharynx Cancers
  – 5,500 men (70%) 2,390 women
Median age at diagnosis was 62 years of age
Mean age at death was 67 years
Relative 5-year Survival Rate is 62% overall:
  - Local: 82%; Regional: 57%; Distant: 35%

How Are These Cancers Being Described?
• Cancers of the Head and Neck
• Squamous Cell Cancers of the Head & Neck
• Cancers of Oral Cavity and Pharynx (OCPC)
  – Lip, (included) salivary glands and nasopharynx (typically excluded)
• Cancers of the Oropharynx
  – A very small subset of Oral Cavity and Pharynx
  – HPV-associated or HPV-non-associated
  – HPV-positive or HPV-negative

HPV-associated vs HPV-positive
HPV-associated means that specific groups of anatomic sites (base of tongue and tonsils) histologically known to be associated with Human Papillomavirus are documented here — it does not reflect actual testing of every specimen from these sites as being positive or negative...

HPV non-associated means that specific groups of anatomic sites (oral cavity and pharynx other than tongue and tonsils) are histologically not known to associated with HPV though every specimen has not been tested.

HPV-positive or HPV negative means that the specimen has been tested and found to either positive or negative for HPV

Approximately 65-75% % of all oropharyngeal cancers (base of tongue and tonsils) are HPV-positive. NOT 100%
Objectives

- Provide an Overview of Oral Cancers, 2013
- Review Anatomy of Sites for Oral Cancers
- Describe the Tools/Website for National and State Surveillance of Oral Cancers
- Examine Trends in Oral Cancers' Epidemiology
- Describe the Role of Human Papillomavirus (HPV) in Cancers of the Oropharynx Region
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Anatomy of Head and Neck

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Oral Cavity and Oropharynx

Tools/Websites for National and State Surveillance of “Oral Cancers”

- NCI – SEER: Surveillance, Epidemiology, & End Results
- CDC – NPCR National Program of Cancer Registries
- NCI/CDC -- State Cancer Profile
- SHA – State Cancer Registry
Tools/Websites for National and State Surveillance of “Oral Cancers”

• NCI – SEER: Surveillance, Epidemiology, & End Results
  Geographic U.S. Areas assessing:
  Incidence rates, Death rates, Trends in rates, (1975-2010)
  Survival and Stage of Diagnosis, Lifetime Risk, Prevalence

• CDC – NPCR: National Program of Cancer Registries
  [www.cdc.gov/npcr/index.htm](http://www.cdc.gov/npcr/index.htm)
  Aggregate & Individual State Cancer Data:
  Cancer Incidence & Mortality (1999-2009);
  Top 10 cancers (national & state ranking);
  State vs National comparisons,
  Selected state cancers by race-gender cateog.

Tools/Websites for National and State Surveillance of “Oral Cancers”

• NCI /CDC: State Cancer Profiles
  U.S., each State, and their Counties assessing:

• State Health Dept: State Cancer Registry
  Each State, and their Counties assessing:
  Death and incidence rates and trends for cancers within states, and their counties
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- Describe the Tools/Websites for National and State Surveillance of Oral Cancers
- **Describe Areas of Surveillance for Oral Cancers**
- Describe the Role of Human Papillomavirus (HPV) in Cancers of the Oropharynx Region
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New Areas of Surveillance

- **Typical**: Oral Cavity & Pharynx Cancers
  - 75% of Head and Neck Cancers
  - Generally tobacco/alcohol risks –
  - HPV non-associated including other and unspecified parts of tongue (excluding base of tongue, gum, floor of mouth, palate, other parts of mouth).
- **New**: Oropharynx Cancers (a subset)
  - 2-4% of Head and Neck Cancers
  - 65%-75% are HPV associated (including base of tongue, lingual tonsil, palatine tonsil, and Waldeyer ring)

HPV-associated vs HPV-positive

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Almost 65-75% % of all oropharyngeal cancers (base of tongue and tonsils) are HPV-positive.

Incidence Rates by Calendar Year for HPV-associated and non-associated Sites 1973-2004

![Incidence Rates by Calendar Year for HPV-associated and non-associated Sites 1973-2004](charturvedi AK et al. / J Clin Oncology 2/1/2008)

New Areas of Surveillance of “Oral Cancers”

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HPV Classification

Over 100 different types of HPV

- **Mucosal HPVs** (oral, genital, ~40 types)
  - **High Risk**: ex. 16, 18
  - **Low Risk**: ex. 6, 11
- **Cutaneous HPVs** (common body warts, ~60 types)
  - Common warts (hands, feet...)
  - Genital and oral warts
  - Low grade cervical changes, Respiratory papillomas


Established Risk Factors for Head and Neck Cancers

- HPV
- Tobacco
- Alcohol

Natural History of HPV Infection

- ~80-85% of people acquire any HPV infection at some point in their lives
- ~90% infections clear in 1-2 years in healthy individuals
- Almost all cervical cancers are caused by HPV infections that persist more than 2 years.

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Almost 65-75% of all oropharyngeal cancers (base of tongue and tonsils) are HPV-positive. NOT 100%


- White male
- White female
- Black male
- Black female

[Graph showing oral cavity and pharynx cancer trends by race-gender per 100,000 population for HPV-associated cancers 1975-1992 & 1992-2008.]

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HPV-Positive Squamous Cell Carcinoma of the Palatine Tonsil

Screening for Oropharyngeal Cancers
(base of tongue, lingual tonsil, palatine tonsil, Waldeyer ring)

- Difficult to detect these at early stage
- No standardized screening tests
  - No oral “PAP” smear to detect cellular changes
  - No FDA approved test for oral HPV infection
- No evidence that detection of oral HPV could be used to predict development of these cancers.

All HPV-associated Cancers, US

Risk Factors for HPV-Positive Cancers

- Associated with lifetime number of vaginal or oral sex partners and open-mouthed kissing
- Compared with HPV-negative cancers, occur more often:
  - Among white men
  - In a population younger by about 4 years (median age 52-56 years)
  - In people who may or may not use tobacco or alcohol

Prevalence of HPV in Oropharyngeal Cancers

- Almost 65%–75% of all oropharyngeal cancers are HPV-positive; 85-95% of these are high risk HPV-16.
- Estimates vary widely depending on:
  - Geographic region.
  - Site
  - Detection method
  - Tissue preservation method
  - Sample size

<table>
<thead>
<tr>
<th>HPV Status</th>
<th>7 US Cancer Registries</th>
<th>Alabama, 2010</th>
<th>Maryland, 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases-known</td>
<td>573 (100%)</td>
<td>59 (100%)</td>
<td>71 (100%)</td>
</tr>
<tr>
<td>HPV Negative</td>
<td>167 (29%)</td>
<td>17 (29%)</td>
<td>21 (30%)</td>
</tr>
<tr>
<td>HPV Positive</td>
<td>406 (71%)</td>
<td>42 (71%)</td>
<td>50 (70%)</td>
</tr>
<tr>
<td>HPV 16/18</td>
<td>349/406 (86%)</td>
<td>25/32 (59%)</td>
<td>29/50 (58%)</td>
</tr>
<tr>
<td>HPV Other</td>
<td>57/406 (14%)</td>
<td>17/42 (41%)</td>
<td>21/50 (42%)</td>
</tr>
<tr>
<td>Overall HPV 16/18</td>
<td>349/573 (61%)</td>
<td>25/59 (42%)</td>
<td>29/71 (41%)</td>
</tr>
<tr>
<td>Cases unknown</td>
<td>81</td>
<td>43</td>
<td></td>
</tr>
</tbody>
</table>

Data source: National Program of Cancer Registries (CDC) and SEER (NCI), covering 99% of US population.
Incidence Rates per 100,000 population for HPV-associated and non-associated Sites U.S., 1973-2004


Counts and Rates of Oropharyngeal Cancer by Site

<table>
<thead>
<tr>
<th>Site</th>
<th>Avg Annual Count</th>
<th>Total Count</th>
<th>Rate/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsils</td>
<td>5,077</td>
<td>20,810</td>
<td>1.6</td>
</tr>
<tr>
<td>Base of Tongue</td>
<td>4,536</td>
<td>18,144</td>
<td>1.4</td>
</tr>
<tr>
<td>Other OP</td>
<td>1,628</td>
<td>6,912</td>
<td>0.5</td>
</tr>
<tr>
<td>Total</td>
<td>11,241</td>
<td>44,966</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Annual Percentage Change Oropharyngeal Cancers, by Site, 1999-2007


Annual Percentage Change in Oropharyngeal cancers, by Sex and Race/Ethnicity, 1999-2007


HPV and Rising Oropharyngeal Incidence in the U.S., 1988-2004

- Incidence of HPV-positives increased by 225% during 1988-2004 -- incidence of HPV-negative cancers declined by 50%.
- Should recent trends continue, the annual number of HPV-positives among men will surpass that of cervical cancers among women by the year 2020.

Source: Chaturvedi A et al., ASCO Annual Meeting, May 2011

Prognosis

- HPV-positive oropharyngeal cancers have improved prognosis/outcomes relative to HPV-negative OPCs.
- HPV-positive tumors have higher survival rates, respond better to radiation and chemotherapy treatment, and are less likely to recur than HPV-negative ones.
- HPV +/− tumor status may drive treatment decisions.
Differences in HPV-Positive Oropharyngeal Cancers by Race/Ethnicity

- HPV-positive oropharyngeal cancers occur more often in whites and are associated with improved outcomes
- Settle, 2009
  - Median overall survival: 70.6 months for whites vs. 20.9 months for blacks
  - HPV positivity in oropharyngeal cancer patients nearly 9-fold higher in whites than blacks

Vaccines – FDA Approval

<table>
<thead>
<tr>
<th>Gardasil</th>
<th>Cervarix</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Types</td>
<td>2 Types</td>
</tr>
<tr>
<td>HPV 6,11,16,18</td>
<td>HPV 16,18</td>
</tr>
<tr>
<td>Females and Males</td>
<td>Females</td>
</tr>
</tbody>
</table>

ACIP Recommendations for HPV Vaccine in the United States

- Quadrivalent vaccine
  - Routine, females 11 or 12 yrs*
  - Catch-up, 13-26 yrs
- Quadrivalent or Bivalent vaccine
  - Routine, females 11 or 12 yrs*
  - Catch-up, 13-26 yrs
- Quadrivalent vaccine
  - May be given, males 9-26 yrs

Potential for HPV Vaccines to Prevent Oral HPV Infection

- Effectiveness to prevent oral HPV infection is unknown.
- High prevalence of HPV-16 in oropharyngeal cancers suggests HPV vaccination may have a major impact on incidence of OPCs.
- Periodic surveillance in HPV-associated oropharyngeal cancers will be important to monitor the impact of HPV vaccines.

Clinical Implications – Tobacco Cessation

- Most Oral Cavity and Pharynx cancers (75%) caused by tobacco and alcohol use
- Expand efforts for tobacco cessation, particularly among black males and females
- Dentists should be aware that younger patients with no tobacco or alcohol use may develop HPV-associated Oral Cavity and Pharynx cancers

Conclusions

- Rates of HPV-positive oropharyngeal cancers are increasing in young, white males.
- HPV-positive oropharyngeal cancers are diagnosed later but have better prognosis than HPV-negative cancers.
- Potential for number of HPV-positive oropharyngeal cancers among men to surpass that of cervical cancers among women by the year 2020.
- HPV vaccines may greatly affect the US public health by preventing non-cervical cancers, such as oropharyngeal cancers.
References


Chaturvedi AK et al. Human Papillomavirus and Rising Oropharyngeal Cancer Incidence in the U.S. http://jcis.aacrjournals.org/content/29/32/4294.abstract
