HPV Vaccination and its Implications in Otolaryngology

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Outline

• Background

• Incidence and Epidemiology

• Cervical Cancer studies and vaccine approval

• ABHACUS (Assessing the Burden of HPV-Associated Cancer in the United States)
  • Following incidence
  • Socioeconomic assessment
  • Mathematical modeling

• Public Policy and Public Health
  • Incidence surveillance results
  • Future studies needed
  • Cost-effectiveness, population targeting, funding
Background

- Squamous cell carcinoma of head and neck
  - 4% of all malignancies in the United States
  - Incidence= 17 per 100,000 persons per year

- HPV-associated cancers
  - 10.6 per 100,000 people per year
  - Estimated 7360 cases in head and neck region per year
  - Head and neck second only to cervical
  - Majority attributable to HPV 16 and 18

- Recurrent Respiratory Papillomatosis
  - HPV6 and 11
  - Though rare, major morbidity especially in children
Oropharyngeal and Oral Cancer

- 35,000 cases projected for 2010
- 10.4 cases per 100,000 persons

1998-2003:
- 44,160 potentially HPV+ cancers
  - 43.6% tonsillar
  - 38.4% base of tongue
  - 18% other oropharyngeal tumors
- 35.6% oropharyngeal are HPV+ (87% HPV-16)
- 23.5% oral cancers are HPV+ (68% HPV-16)

Males > females (3-4:1)

Defined as overlapping lesion of tongue; lateral wall of oropharynx; overlapping lesion of oropharynx; oropharynx, NOS; pharynx, NOS; overlapping lesion of lip, oral cavity and pharynx.

Oropharyngeal and Oral Cancer

- Most common in or after 50’s
- Race/ethnicity
  - Blacks > whites
  - Non-Hispanics > Hispanics
- Increase in HPV-associated cancers in this region despite decrease at other sites
  - Decreased tobacco exposure
  - Sexual behavior
    - Increased risk with >6 partners, >4 oral sex partners, earlier age at first intercourse in men
Laryngeal Cancer

- 12,720 cases projected for 2010
- 3.4 per 100,000 persons
- Greatest risk factors:
  - Alcohol, tobacco
  - HPV-association investigated
    - Identified in 3.3-50% of biopsies from separate studies
- Males > females (5:1) – previously 15:1
- Peak incidence 50-60 yrs
- Blacks > whites
Recurrent Respiratory Papillomatosis

- 1500-2500 new cases each year

- Children
  - 4.3 cases per 100,000 children
  - Peak at 2-3 yrs
  - Often firstborn of young mothers of low economic status
  - Male = female

- Adults
  - 1.8 per 100,000 in adults
  - Peak at 20-40 yrs
  - Males > females (4:1)
Recurrent Respiratory Papillomatosis

- HPV 6 and 11

- Acquisition
  - Upper aerodigestive tract exposure to mother with HPV infection
  - Some born to mothers with HPV do not acquire RRP
  - Cesarean delivery of child who developed RRP
Cervical Cancer Basics

- HPV as necessary cause of cervical cancer 1995/1996
- FUTURE II Study Group phase 3 trial, 2003-2006
  - RCT of 12,167 females, 15-26 yrs
  - Quadrivalent (HPV6,11,16,18) vaccine had 98% efficacy
- Quadrivalent and bivalent (HPV16 and 18) FDA-approved
  - Females aged 9-26
  - 3-dose schedule starting at age 11 (ideal before sexual contact)
  - Prevention of cervical cancer and genital warts
- Males 9-26 yrs
  - Quadrivalent approved by FDA March 2010
  - However, not deemed cost-effective
  - More cost-effective to vaccinate >80% females

NOTES: Study to approve bivalent vaccine? Where is the best place for this slide?!?!
ABHACUS

- Assessing the Burden of HPV-Associated Cancer in the United States

- Goals are to monitor:
  - Age-specific rates of HPV-associated cancers
    - CDC National Program of Cancer Registries (NPRC)
    - NCI Surveillance, Epidemiology and End Results (SEER)
  - Age-specific rates of HPV-associated cancer precursors
  - Distribution of associated HPV types
  - Incidence of carcinoma precursors and invasive carcinoma along with prevalence of vaccination
  - Methods of linking screening and risk factor data that are already being collected by other surveillance data

“"To systematically monitor age-specific rates of invasive cervical cancer and other invasive HPV-associated cancers.
To systematically monitor age-specific rates of cervical cancer precursors and precursors for other HPV-associated cancers.
To identify the distribution of HPV types associated with HPV-associated carcinoma precursors and invasive carcinoma.
To monitor the incidence of carcinoma precursors and invasive carcinoma along with prevalence of vaccination.
To explore and evaluate methods of linking screening and risk factor data that are already being collected by other surveillance data."
ABHACUS

  - 10,800 HPV-associated cervical cancers occurred per year—more than any other site.
  - Nearly 7,400 potentially HPV-associated cancers of the oral cavity and oropharynx per year; male-to-female ratio 3.3:1.
  - More than 3,000 HPV-associated anal cancers per year.
  - About 2,300 new cases of vulvar cancer each year.
  - Penile cancer relatively rare—about 800 men each year.
  - About 600 women per year developed vaginal cancers.

ABHACUS

- “HPV-associated”
  - HPV presence vs. activity vs. oncogenesis
  - Positive PCR amplification ≠ cancer
  - Not completely valid assumption but will lead to more studies
  - Additive/synergistic effect of HPV on tobacco or alcohol use
  - Cervical cancer studies ongoing for at least two decades before vaccine trials

- RRP
  - HPV 6,11 present in more patients than RRP, suggesting additional factors
Socioeconomic Status

• SES important information for allocating resources

• Oral cavity and oropharyngeal cancer
  • Overall incidence rates:
    • Increased $\rightarrow$ Higher education, low-level to mid-level income, and residence in metropolitan or suburban areas
    • Decreased $\rightarrow$ 10-20% poverty status
  • Female incidence rates:
    • Decreased $\rightarrow$ Hispanics, Asian/Pacific Islanders, rural residence
    • Counties with high school education rates 75% -<85% $\rightarrow$ lower incidence rate than those with >85% high school education
Socioeconomic Status

- Male incidence rates:
  - Decreased $\rightarrow$ Hispanics and those in a county with <85% high school education
  - Increased $\rightarrow$ Higher county smoking prevalence and residence in a county with lower median household income

- Ethnicity and rural-urban incidence rates:
  - Asian/Pacific Islanders $\rightarrow$ rural $>$ metropolitan areas
  - Whites $\rightarrow$ metropolitan $>$ rural counties
  - Blacks $\rightarrow$ significantly higher incidence rates compared with whites in metropolitan and especially rural areas
  - Asian/Pacific Islanders $\rightarrow$ decreased incidence rate compared with whites in metropolitan areas

- Current smoking $\rightarrow$ increased incidence rates
Years of Potential Life Lost and Productivity Costs

- **Cancer-specific estimates (2003)**
  - 45,815 YPLL for oral cavity/oropharyngeal cancer in M (lowest was 3,654 YPLL for penile cancer)
  - 17,773 for oral cavity/oropharyngeal in F (range of 5,199 YPLL for vaginal cancer to 89,936 YPLL for cervical cancer)

- **Mortality costs (2003)**
  - Used data on US mortality, life tables, annual earnings, household services, labor force participation rate
  - **$1.1 billion**: oral/oropharyngeal cancer in males
  - **$270 million**: oral/oropharyngeal cancer in females
  - (Cervical cancer highest cost at $1.8 billion)
Years of Potential Life Lost and Productivity Costs

- Total mortality costs of all HPV-associated cancers in white non-Hispanics
  - 44.2% cervical cancer
  - 40.9% oral cavity and oropharyngeal cancer
  - 5.8% anal cancer

- Drawbacks
  - Information on race-specific earnings was not incorporated
  - Pain, suffering, and psychosocial costs were not accounted for
  - Society’s value on an individual cannot be calculated
  - Estimates apply to HPV-associated cancers, not the percentage specifically caused by HPV
  - No direct and indirect medical costs, or caregiver costs
Public Policy and Public Health

- Before recommendation and funding for vaccine
  - Incidence surveillance results
    - How long?
    - What is a significant result?
  - RRP
    - Monitor as a separate entity to note change in burden of disease
    - Prospective study in infants difficult, but if no change after administration to mothers, would have to consider at-birth vaccination approval, as in Hepatitis B
Public Policy and Public Health

- Before recommendation and funding for vaccine cont’d
  - Cost-effectiveness studies for males and females
  - Resource allocation
    - Determine populations with higher burden
    - Repeat SES studies when HPV causation established?
  - Establish oncogenic causation by HPV in head and neck cancers
    - “…Laboratory-based assays should include demonstration of the specificity of the viral DNA in tumor cell nuclei, detection of viral oncogene expression, demonstration of a clonal association between virus and tumor (eg, integration, viral load, variant analysis), and dependence of the malignant phenotype upon viral gene expression.”
Public Policy and Public Health

• Even if these goals are accomplished...
  • Original HPV debate of cost, safety, right to refuse, and moral issues
  • HPV-associated cancers sexual practice issue reminiscent
    • Link to higher number of sex partners and oral sex partners
    • HPV prevalence in cervical tissue, higher rate of oropharyngeal cancer in men
    • Increased rate of tonsillar cancer in men with wives with cervical dysplasia or cancer
    • Some with oropharyngeal cancer report few partners and no oral sex partners
    • What other populations might be at higher risk because of sexual practices?
Public Policy and Public Health

- **Funding**
  - Vaccine available through Vaccines for Children (VFC) in all 50 states; how will new data change funding through SCHIP, Medicaid; for uninsured and requirements for insurance companies
  - What criteria would make an adult eligible for vaccine coverage
  - Will depend on cost-effectiveness studies

- **Vaccine as a requirement vs. option**
  - Washington, DC made vaccine a school requirement in 2007
  - 41 other states with laws for education and funding
  - If it protects against HPV-associated cancers and possibly RRP, should it be required at birth or as part of the vaccination series?
Summary

- Oral cavity and oropharyngeal cancer, laryngeal cancer, RRP are true disease burdens
- To be monitored after advent of HPV vaccine
- Further studies on causality of HPV in these cancers
- Public policy and public health issues
  - Vaccine expansion to boys, adults
  - At-risk populations?
  - Evidence of cost-effectiveness to support funding
  - Legislation on administration
References


• Center for Disease Control and Prevention. “FDA Licensure of Bivalent Human Papillomavirus Vaccine (HPV2, Cervarix) for Use in Females and Updated HPV Vaccination Recommendations from the Advisory Committee on Immunization Practices (ACIP)” *Weekly* 2010 59(20):626-629 Website: [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a4.htm?s_cid=mm5920a4_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a4.htm?s_cid=mm5920a4_e)

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