HPV-Associated Disease and Prevention
Odessa Regional Medical Center
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Erich M. Sturgis, MD, MPH
Professor
Department of Head & Neck Surgery
Department of Epidemiology
Christopher & Susan Damico Chair in
Viral Associated Malignancies

No C.O.I., disclosures, or off-label
Outline

- Pathophysiology
- Epidemic
- Prevention
- Screening
2008 Nobel Prize in Physiology or Medicine

Harold zur Hausen, M.D.
Mucosal sites of infection

~ 40 HPV Types

Cutaneous sites of infection

~ 80 HPV Types

High risk (oncogenic) HPV 16, 18 most common

Low risk (non-oncogenic) HPV 6, 11 most common

Genital Warts
Laryngeal Papillomas
Low Grade Cervical Disease

“Common” Cutaneous Warts

Anogenital & Oropharyngeal Cancers
Cancer Precursors:
Anogenital High Grade Dysplasias

Laryngoscope 2010
Cancers Attributed to HPV

Anogenital Cancers

Estimated, %

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Estimated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal</td>
<td>70</td>
</tr>
<tr>
<td>Vulvar</td>
<td>50</td>
</tr>
<tr>
<td>Vaginal</td>
<td>50</td>
</tr>
<tr>
<td>Penile</td>
<td>50</td>
</tr>
<tr>
<td>Cervical</td>
<td>95</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>72%</td>
</tr>
</tbody>
</table>
H&N Squamous Cell Carcinomas

- Nasopharynx
- Oropharynx: soft palate, tonsil, base of tongue, post pharyngeal wall
- Hypopharynx
- Larynx
- Oral Cavity
- Nose/Paranasal Sinuses
Benign Diseases Attributed to HPV

Each Year in the U.S.:
- 1.4 million new cases of CIN 1
- 1 million new cases of genital warts
- 330,000 new cases of CIN 2-3

Prevalence of HPV 6 & 11

- CIN 1: 0%
- VIN 1: 20%
- Genital Warts: 60%
- RRP: 100%
Genital HPV Infection

Most females & males will be infected with at least one HPV type at some point

- 80 million Americans currently infected
- 14 million new infections/year in the US
- the most common “STD”
- most are asymptomatic
- most common in teens & early 20s

HPV Prevalence among Women by Age (with normal cytology)

HPV prevalence among women with normal cytology by age group (years). Shaded area reflects 95% confidence intervals. C: Caribbean, Redrawn from Bruni L et al.

D. Forman et al. Vaccine 2012
Oral HPV prevalence by age

Men, any HPV infection

Women, any HPV infection

High-risk HPV types

Low-risk HPV types
Outline

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- Epidemic
- Prevention
- Screening
Global Burden of Cervical Cancer

- 2015: 1 in 6 live in Africa
- 2050: 1 in 4
- 2100: 2 in 5

(Gerland, P et al. Science 2014)


J Natl Cancer Inst 2013


J Natl Cancer Inst 2013


* J Natl Cancer Inst 2013
Epidemic of HPV Cancers in U.S. Men

Age-Adjusted SEER Incidence Rates
By Cancer Site
All Ages, White, Male
1975–2012 (SEER 9)

- Oropharynx (tongue base): +5%
- Oropharynx (tonsil): +5%
- Anus: +3%
- Penis: < 1/100,000
HPV Cancers in U.S. Women

- Vulva: APC: +1%
- Anus: +3%
- Vagina
Newly Diagnosed-Utreated Cases Presenting to MD Anderson Each Year

Number of Cases

- Oropharynx
- Cervix
- Anus
- Vulva
- Penis
- Vagina

Year:
- 1990
- 1991
- 1992
- 1993
- 1994
- 1995
- 1996
- 1997
- 1998
- 1999
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
- 2011
- 2012
- 2013

Number of Cases:
- 0
- 50
- 100
- 150
- 200
- 250
- 300
- 350
Outline

- Pathophysiology
- Epidemic
- Prevention
- Screening
HPV Prophylactic Vaccines

- Recombinant L1 capsid proteins that form “virus-like” particles
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection
# HPV Vaccines Currently Licensed in U.S.

<table>
<thead>
<tr>
<th></th>
<th>Bivalent 2vHPV (Cervarix)</th>
<th>Quadrivalent 4vHPV (Gardasil)</th>
<th>9-Valent 9vHPV (Gardasil 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>GSK</td>
<td>Merck</td>
<td>Merck</td>
</tr>
<tr>
<td>HPV Types Included</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Hypersensitivity to latex*</td>
<td>Hypersensitivity to yeast</td>
<td>Hypersensitivity to yeast</td>
</tr>
<tr>
<td>Dose Schedule</td>
<td>3 dose series: 0, 1, 6 months</td>
<td>3 dose series: 0, 2, 6 months</td>
<td>3 dose series: 0, 2, 6 months</td>
</tr>
</tbody>
</table>
HPV Vaccine Comparison

HPV Types Included in Vaccine

<table>
<thead>
<tr>
<th></th>
<th>6</th>
<th>11</th>
<th>16</th>
<th>18</th>
<th>31</th>
<th>33</th>
<th>45</th>
<th>52</th>
<th>58</th>
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<tr>
<td>Bivalent</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Quadrivalent</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>9-valent</td>
<td></td>
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</tbody>
</table>

- **Bivalent**
  - Genital warts
  - ~66% of Cervical Cancers
  - ~90% of HPV+ Anal & Oropharyngeal Cancers

- **Quadrivalent**
  - Cervical Cancers
  - ~15% of Cervical Cancers
HPV Vaccine Recommendation

Girls and Boys can start HPV vaccination at age 9

Preteens should finish HPV vaccine series by 13th birthday

**Catch-up Vaccination:**
- girls 13-26 years old who have not started or finished HPV vaccine series
- boys 13-21 years old who have not started or finished HPV vaccine series
HPV Vaccination Is Safe, Effective, and Provides Lasting Protection

• SAFE
  – Benefits far outweigh any potential risks
  – Similar to safety reviews of MCV4 and Tdap vaccination

• EFFECTIVE
  – Population impact against early and mid outcomes are already being reported in multiple countries

• LASTING PROTECTION
  – No evidence of waning protection

Association of Varying Number of Doses of Quadrivalent Human Papillomavirus Vaccine With Incidence of Condyloma

Eva Herweijer, MSc; Amy Leval, PhD; Alexander Ploner, PhD; Sandra Eloranta, PhD; Julia Fridman Simard, ScD; Joakim Dillner, MD; Eva Netterlid, PhD; Pär Sparén, PhD; Lisen Arnhem-Dahlström, PhD

DESIGN, SETTING, AND PARTICIPANTS An open cohort of all females aged 10 to 24 years living in Sweden (n = 1 045 165) was followed up between 2006 and 2010 for HPV vaccination and first occurrence of condyloma using the Swedish nationwide population-based health data.
Reduced Prevalence of Oral Human Papillomavirus (HPV) 4 Years after Bivalent HPV Vaccination in a Randomized Clinical Trial in Costa Rica

Rolando Herrero¹*, Wim Quint², Allan Hildesheim³, Paula Gonzalez⁴, Linda Struijk², Hormuzd A. Katki³, Carolina Porras⁴, Mark Schiffman³, Ana Cecilia Rodriguez⁴, Diane Solomon⁵, Silvia Jimenez⁴, John T. Schiller⁶, Douglas R. Lowy⁶, Leen-Jan van Doorn², Sholom Wacholder³, Aimée R. Kreimer³ for the CVT Vaccine Group

<table>
<thead>
<tr>
<th>Arm</th>
<th>Number of women</th>
<th>Number of women with infection</th>
<th>Prevalence</th>
<th>95%CI</th>
<th>Vaccine efficacy 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Infections</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV16/18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>2910</td>
<td>1</td>
<td>0.0</td>
<td>0.00:0.2</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2924</td>
<td>15</td>
<td>0.5</td>
<td>0.3:0.8</td>
<td>93.3%</td>
</tr>
<tr>
<td>HPV16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>2910</td>
<td>1</td>
<td>0.0</td>
<td>0.00:0.2</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2924</td>
<td>12</td>
<td>0.4</td>
<td>0.2:0.7</td>
<td>91.6%</td>
</tr>
<tr>
<td>HPV18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>2910</td>
<td>0</td>
<td>0.0</td>
<td>0.00:1</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2924</td>
<td>4</td>
<td>0.1</td>
<td>0.0:0.3</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Cervical Infections</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV16/18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>2910</td>
<td>61</td>
<td>2.1</td>
<td>1.6:2.7</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2924</td>
<td>219</td>
<td>7.5</td>
<td>6.6:8.5</td>
<td>72.0%</td>
</tr>
</tbody>
</table>
FIGURE. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17 years, by survey year — National Immunization Survey-Teen, United States, 2006–2013

Abbreviations: Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; MenACWY = meningococcal conjugate; HPV = human papillomavirus.
* ≥1 dose Tdap vaccine on or after age 10 years.
† ≥1 dose MenACWY vaccine.
TABLE 2. Top five reasons for not vaccinating adolescents with human papillomavirus (HPV) vaccine* — National Immunization Survey-Teen, United States, 2013

<table>
<thead>
<tr>
<th>Reason</th>
<th>Parents of girls</th>
<th>(95% CI)</th>
<th>Reason</th>
<th>Parents of boys</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of knowledge</td>
<td>15.5</td>
<td>(13.0–18.5)</td>
<td>Not recommended</td>
<td>22.8</td>
<td>(20.6–25.0)</td>
</tr>
<tr>
<td>Not needed or necessary</td>
<td>14.7</td>
<td>(12.5–17.3)</td>
<td>Not needed or necessary</td>
<td>17.9</td>
<td>(15.9–20.1)</td>
</tr>
<tr>
<td>Safety concern/Side effects</td>
<td>14.2</td>
<td>(11.8–16.8)</td>
<td>Lack of knowledge</td>
<td>15.5</td>
<td>(13.7–17.6)</td>
</tr>
<tr>
<td>Not recommended</td>
<td>13.0</td>
<td>(10.8–15.5)</td>
<td>Not sexually active</td>
<td>7.7</td>
<td>(6.4–9.2)</td>
</tr>
<tr>
<td>Not sexually active</td>
<td>11.3</td>
<td>(9.1–13.9)</td>
<td>Safety concern/Side effects</td>
<td>5.9</td>
<td>(5.6–8.5)</td>
</tr>
</tbody>
</table>

Abbreviation: CI = confidence interval.

* Analysis limited to parents reporting that they were not likely to seek HPV vaccination for their teen in the next 12 months or were unsure of their HPV vaccination plans.
13-17yo Girls in 2013: 38%
13-17yo Boys in 2013: 14%

Percentage of adolescent girls who received 3 doses of HPV vaccine

- Red: 17.6–25.4
- Orange: 25.5–32.0
- Yellow: 32.1–40.3
- Light yellow: 40.4–55.1
Outline

- Pathophysiology
- Epidemic
- Prevention
- Screening
George Papanikolaou (1883-1962)
annual burden of genital HPV-related disease (U.S. females)

- 4,100 cervical cancer deaths
- 12,900 new cases of cervical cancer
- 330,000 new cases of HSIL: CIN2/3 (high grade cervical dysplasia)
- 1 million new cases of genital warts
- 1.4 million new cases of LSIL: CIN1 (low grade cervical dysplasia)

3 million cases & $7 billion
Trends in Cancer Incidence & Number
Oropharynx vs. Cervix

Chaturvedi AK, et al.
JCO 2011.
Cervix

Median Age at Presentation:

45yo

Oropharynx

55yo
Conclusions

- HPV cancer epidemic – oropharyngeal, anal, & vulvar
- HPV vaccination is imperative: Further Delay = Exponential Costs & Suffering
- Without novel screening/treatment of premalignancy: 30 years of increasing incidence
Thank You

esturgis@mdanderson.org

George Harrison
1943 - 2001
Oropharynx Cancer