HPV Vaccination: A Missed Opportunity for Cancer Prevention

Kevin A. Ault, MD
National Title X Reproductive Health Conference
July 16, 2018
COI disclosure etc

• I have no conflicts of interest with this talk.
• Clinical recommendations concerning HPV vaccination are consistent with ACIP recommendations, which closely match FDA labeling.
• I act as an advisor to ACOG and NCI on this topic.
Objectives

• Recognize dosing and related clinical recommendations for routine use of the HPV vaccine.
• Acquire an appreciation for the multiple cancers prevented by this vaccine
• Explain “best practices” to increase HPV vaccination rates in office practice.
Tragedy is a tool for the living to gain wisdom, not a guide by which to live.

Kansas State University on March 18, 1968 as part of the Alfred M. Landon Lectures on Public Issues.

About one-fifth of the people are against everything all the time.

University of Pennsylvania on May 6, 1964
# Infections and Cancers: Global Burden

<table>
<thead>
<tr>
<th>Infection</th>
<th>Cancer</th>
<th># cases worldwide</th>
<th>% worldwide</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. pylori</em></td>
<td>stomach</td>
<td>490,000</td>
<td>5.4</td>
</tr>
<tr>
<td>HPV</td>
<td>Cervix etc</td>
<td>550,000</td>
<td>6.1</td>
</tr>
<tr>
<td>Viral hepatitis</td>
<td>Liver</td>
<td>390,000</td>
<td>4.3</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td>1.6 million</td>
<td>17.7</td>
</tr>
</tbody>
</table>

Source – World Health Organization
WHO – Cervical Cancer Mortality 2012
New Developments concerning HPV vaccine

- a “second generation” polyvalent HPV became available for use in 2016
- Increased emphasis on male cancers
- “Maturing” data concerning efficacy and safety
- HPV vaccine uptake remains low especially in Kansas, Missouri & Oklahoma
- Evidence based, “best practices” for increasing vaccine uptake
The squamo-columnar junction marks the transition from a *stratified squamous* to a *glandular* epithelium.

- **Cutaneous HPVs**
- **Epidermodysplasia verruciformis HPV**
- **Mucosal/Genital HPVs (low-risk)**
- **Mucosal/Genital HPVs (high-risk)**

Slide courtesy of Dr. William Bonnez, University of Rochester
HPV Types Differ in their Disease Associations

~40 Types

Mucosal sites of infection

- High risk (oncogenic)
  - HPV 16, 18 most common
  - Cervical Cancer
  - Anogenital Cancers
  - Oropharyngeal Cancer
  - Cancer Precursors
  - Low Grade Cervical Disease

Low risk (non-oncogenic)
- HPV 6, 11 most common
- Genital Warts
- Laryngeal Papillomas
- Low Grade Cervical Disease

~ 80 Types

Cutaneous sites of infection

- "Common"
  - Hand and Foot Warts
HPV Infection

Almost all females and males will be infected with at least one type of HPV at some point in their lives

- Estimated 79 million Americans currently infected
- 14 million new infections/year in the US
- HPV infection is most common in people in their teens and early 20s

Most people will never know that they have been infected

HPV 6/11/16/18 Prevalence in Females by Age, USA

Markowitz et al 2016 (NHANES data)
Summary of current ACIP recommendations – 2015-16 update

- routine vaccination of adolescent females and males aged 11–12 years with 2 doses of HPV vaccine. The vaccination series can be started as young as age 9 years.
- If over age 15 at initiation, three doses over 6 months
- “Catch up” to age 26
- Current version is 9 valent

See [http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv](http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv) or MMWR
# HPV Vaccine Comparison

## HPV Types Included in Vaccine

<table>
<thead>
<tr>
<th>HPV Vaccine</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>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadrivalent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-valent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### These HPV Types Cause:
- Genital warts
- ~66% of Cervical Cancers
- ~15% of Cervical Cancers

HPV Types that Cause Cervical Cancer

Percent of cervical cancers worldwide caused by HPV type

- **HPV 16**
- + **HPV 18**
- + **HPV 45**
- + **HPV 31**
- + **HPV 33**
- + **HPV 52**
- + **HPV 58**

Top cancer-causing types of HPV

- HPV 16
- HPV 18
- HPV 45
- HPV 31
- HPV 33
- HPV 52
- HPV 58

De San Jose *et al* 2010
HPV Vaccine – Ten plus Years of Data

• **Efficacy** – first data are available showing protection against cancer

• **Safety** – large systematic review, and initial data concerning 9 valent vaccine reassuring.

• **Uptake** – provider recommendation, “multi” interventions, “Announcement”
External Genital Warts - Diagnosis by Age Australia

Rates of precancerous lesions in Victoria, Australia
U.S. population of young adults (ages 18-33 years): Lower oral HPV prevalence in vaccinated men and women

Oral HPV prevalence for HPV 6/11/16/18 ~4 years after self-reported receipt of at least 1 vaccine dose

Prevalence %

Females

Males

Vaccinated

Unvaccinated

Chaturvedi, JCO 2017
HPV Vaccine Efficacy

• Review of 58 studies in nine countries shows efficacy against initial HPV infection, genital warts, and precancerous/dysplastic changes

• Danish study showed 90 % effectiveness against precancerous cervical disease over ten years

• Recent Finnish shows zero HPV related cancers at all anatomic sites

Potential Impact of HPV9 Vaccine – USA 2015 by cancer site

Saraiya et al. 2015
Predominance of oropharynx cancers in males

Observed incidence of HPV-positive oropharynx cancer

Projected incidence of oropharynx cancer

Projected incidence rates
- Most common HPV+ cancer
- 2030: Most common head and neck cancer
- Majority among men

Chaturvedi, JCO 2011
Higher oral HPV prevalence in men than women
United States, NHANES 2009-2012

Gillison, JAMA 2012; Chaturvedi, Cancer Res 2015
An excess of Southern attorneys: an unappreciated cause of home accidents.

From the website “Spurious Correlations”
97% correlation
Safety of HPV Vaccines

• Review of 109 studies with 2.5 million subjects showed to link to autoimmune or neurological diseases

• Nine valent vaccine safety reviewed at recent CDC ACIP meeting, similar to prior versions

• Main side effects – site reactions and syncope

Source: Philips et al 2017
Vaccination Rates for Adolescent Vaccines, 2006-2016 United States

Data from CDC MMWR August 2017
HPV Vaccination Rates by State

EXHIBIT 4: STATES WITH THE HIGHEST AND LOWEST RATES OF FIRST-DOSE HPV VACCINATION (2016)

Data via CDC, graphic via Blue Cross / Blue Shield
Systematic Review of Interventions to Increase HPV Vaccination Rates

- Best predictor – provider recommendation
- Other effective - remind and recall, patient education, provider assessment and feedback
- Multi-component interventions likewise effective
- Ineffective - school based, provider reminders only, “mandates”

Smulian et al 2016
9 to 16% increase in first dose coverage in “announcement” group

Brewer et al 2016
Major Weaknesses of Provider Recommendations

• “Risk based” strategies
• Lack of urgency (delayed to future visit)
• Weaker recommendation for males
• Correlation of high quality recommendation – a) child is due for adolescent vaccines b) strong recommendation c) prevents multiple cancers and d) elicit questions

Gilkey et al 2015
“Secondary acceptance” of HPV Vaccine

- 45% of those parents who initially declined will accept before age 17
- Acceptance associated with provider recommendation and further information about HPV vaccination
- Only 53% reported further discussion with providers

Kornides et al 2018
Priority Areas for Implementation Research

• Social media interventions
• Provider in clinic quality improvement
• Health care payors “best practices”
• Social media mythology
• Interventions in rural areas

Reiter et al 2018
Conclusions

• Many HPV related cancers on the rise
• Newest version of the HPV vaccine could prevent 90 % of cervical cancers
• Provider recommendation best predictor of HPV vaccine uptake
• Future developments – emphasis on males, implementation research & social media
“Thank you ever so much”

Any questions?

Kevin A. Ault, MD
Department of Obstetrics and Gynecology
3901 Rainbow Blvd
University of Kansas Medical Center
Kansas City KS USA 66160
kault2@kumc.edu or Twitter @kevinault