The Second Cancer Vaccine: Human Papillomavirus Vaccine

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Disclosures

I have no disclosures.

I do not plan to discuss off label uses of vaccines.

Objectives

• Discuss the epidemiology of human papillomaviruses (HPV)
• Explain the link between HPV and cancers
• Counsel a family regarding the HPV vaccines

Human Papillomaviruses

DNA viruses, family Papovaviridae
Over 100 types
Specialized for epithelia
Not cytotoxic, viral genes promote replication and delay differentiation, leads to proliferative lesions (warts)
Benign skin
Keratinized epithelium
Palmar and plantar warts
HPV 1 and 2
No cancers recognized

Epidermodysplasia verruciformis
Keratinized epithelium
Flat warts and subclinical
HPV 5 and 8
Inherited disorder of cell mediated immunity
Skin cancers common, squamous cell

Genital warts
Genital epithelium and mucosa
Warts
HPV 6 and 11
No cancers recognized
Respiratory papillomatosis in children

High-risk genital
Genital epithelium and mucosa
Flat warts or subclinical
HPV 16, 18, 31, 45
Cervical dysplasia and cancer
Anal intraepithelial neoplasms
Oropharyngeal cancers
**HPV Epidemiology**

- Spread person to person by close contact
- Asymptomatic people can transmit
- Anogenital – over 40 types, sexual spread
  - Over 40% of adolescents infected
- Regular condom use does decrease risk
- Incubation unknown, probably months to yrs

**Clinical illnesses**

- Warts: skin, flat
- Condylomata acuminate: anogenital warts
- Respiratory papillomatosis
- Epidermodysplasia verruciformis
- Oncogenic potential on mucous membranes

**Cancers**

- Cervical: Adolescents at higher risk
  - Low-grade: LSIL, CIN 1
  - High grade: HSIL, CIN 2/3
- Dysplasia usually resolves without therapy
- Skin: immunocompromised only

**Other Cancers**

- Anogenital: anus, vulvar and penile
- Oropharyngeal: tonsils, base of tongue
- Laryngeal and lung cancers unusual
- Skin cancers in immunocompromised
HPV Vaccines

Virus-like particles genetically engineered
Capsid proteins produced; form shells
Gardasil: recombinant *Saccharomyces*
Cervarix: recombinant baculovirus in *Trichoplusia ni* insect cells

Three dose series
Zero, 1 month, 6 months
Well tolerated
Pain at injection site, fainting
Highly immunogenic
Highly protective

Gardasil (Merck)
Quadrivalent types 6, 11, 16, 18
Immunogenic in girls and
100% effective against persisting infection
Immunogenic and effective in boys
Licensed for girls and boys, start age 11-12 yr

Cervarix (GSK)
Types 16 and 18
Immunogenic and highly effective in females
No studies in males
Novel production: baculovirus vector, insect
Novel adjuvant: ASO4 adsorbed onto AlOH3
Recommendations

Universal for girls and boys
Gardasil: girls and boys starting age 11-12
Catch up recommended through age 26 y for females, 21 for males
Cervarix: licensed only for girls, same ages

Websites

www.aap.org
www.cdc.gov
www.immunizationinfo.org
www.vaers.org

Smiling is a contagious condition!
Based on the slides for the CDC’s HPV Speaker’s Bureau

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Kansas City, MO
Funded by a grant from CDC to AAP

National Estimated Vaccination Coverage Levels Among Adolescents 13-17 Years, NIS-Teen, 2006-2012

"But adolescents just don't make office visits!"

Actual and Potentially Achievable Vaccination Coverage if Missed Opportunities Were Eliminated
NIS-Teen, 2012

This talk is designed to help you be able to:

1. Employ communication strategies on a daily basis to aid parents in making a decision to vaccinate their children against HPV
2. Answer FAQs about HPV vaccination with accurate, succinct, and compelling responses
3. Explain the critical role of health care team to communication with parents to increase the likelihood of the patient’s full protection with HPV vaccination
Objective #1

**A PRACTICAL IMMUNIZATION COMMUNICATION STRATEGY**

Developed by Vax Northwest – a Seattle-based collaborative

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**Recommend**

Introduce the topic by clearly stating your recommendations for the immunizations that are due today.

Treat HPV just like the other routinely recommended adolescent immunizations.

- I think Quinn should get 3 shots today: HPV vaccine, meningococcal vaccine and Tdap vaccine.
- I think Michelle should have 3 shots today that will protect her from the cancers caused by HPV, and infections causing meningitis, whooping cough, tetanus, & diphtheria.

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**Ask (Use open-ended questions)**

Ask what questions they have about the vaccines or the schedule.

*What questions do you have for me about these vaccines?*

Clarify and re-state their concerns to make sure you understand.

*It sounds like you’re concerned that the HPV vaccine isn’t necessary because Emily is a virgin. Am I understanding this?*

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**Acknowledge – Strategy for “Accepting Parent”**

Support the parent’s decisions to follow the recommended schedule.

*I think staying up to date with the adolescent vaccines is a great step to take.*

*Keeping Sophie up to date on vaccines is the single most important way our office can work with your family to keep her protected from serious diseases.*
Acknowledgment – Strategy for “Hesitant Parent”

Acknowledge the parent’s concerns
There are a lot of different opinions about vaccines and a lot of conflicting information...

Make clear your goal is the same as the parents
I know you want to do everything you can to keep Sophie safe, and so do I

Name the emotions you observe
Be clear that you are concerned for the health of the adolescent, not just public health safety

Advising:

• Address the parent’s specific concerns
• Offer to assist them to get information relevant to their concerns
• Allow them time to reflect, consult with their spouse/partner
• Provide them with an opportunity to revisit their concerns with you
• Develop a plan that is acceptable to the parent, noting you understand that the decision and burden of responsibility is theirs
• Schedule a follow-up appointment

Top 5 reasons for not vaccinating daughter among parents with no intention to vaccinate in the next 12 months, NIS-Teen 2012

- Not sexually active
- Lack of knowledge**
- Safety / side effects
- Not recommended by provider
- Not needed/necessary

* Not mutually exclusive.
** Did not know much about HPV or HPV vaccine.
FAQ 1: (Didn’t know much about HPV)

**Why is this vaccine needed?**

--**What is HPV?**

--**Is HPV common?**

--**How is HPV spread?**

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**U.S. HPV Prevalence & Incidence Versus Recognition**

- **US statistics**
  - Currently infected ~79 million
  - New infections/year ~14 million
  - HPV infection is most common in people in their teens and early 20s
  - HPV is the most common STI, but most people never know that they have been infected –
    - Female: abnormal pap test w/ positive HPV test
    - Male: no commercially available test

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**Average # of Cancers & Genital Warts Per Year Attributed to HPV Infections, U.S.**

*President’s Cancer Panel Annual Report 2012-2013*

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**How is HPV spread?**

- HPV exposure can occur with any type of intimate sexual contact, not just intercourse

- Among a cohort of adolescent women without prior vaginal intercourse (followed longitudinally):
  - HPV was detected in 46% of females prior to 1st vaginal sex
  - 70% of these women reported non-coital behaviors that may in part explain genital transmission

- Condoms do not completely stop HPV transmission

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*President’s Cancer Panel Annual Report 2012-2013*
Transmission During Intercourse

- Nearly 50% of high school students have already engaged in sexual (vaginal-penile) intercourse
- 1/3 of 9th graders and 2/3 of 12th graders have engaged in sexual intercourse
- 24% of high school seniors have had sexual intercourse with 4 or more partners
- About 50% of people are infected with HPV within 12 months of sexual debut

Try saying:

The virus can spread without intercourse. Even virgins can be infected with HPV.

HPV is so common that almost everyone will be infected at some point. Yet most people never know that they have had an HPV infection.

Even if your child waits until marriage to have sex, he/she could still be exposed if his/her future partner engaged in any type of sexual activity before marriage.

About 79 million Americans are infected with HPV and there are 14 million new infections each year.

FAQ 2: Why give this at 11 or 12 years of age?

Rationale for HPV vaccination at 11-12 years of age

- Optimal vaccine efficacy is derived if the vaccine series is received before onset of sexual activity. (The vaccine is inactive against previously acquired HPV types.)

- Antibody responses are highest at ages 9 through 15 years.

http://pediatrics.aappublications.org/content/129/3/602.full
Rationale for vaccinating early: 
Protection prior to exposure to HPV

Will protection last?

- Efficacy against infection and cervical lesions from HPV strains 16 & 18 -- shown up to
  - 8.4 years with the bivalent vaccine
  - 5 years with the quadrivalent vaccine
- Ongoing monitoring is essential so we will know if a booster is needed

Long term protection against cervical infection with the human papillomavirus: review of currently available vaccines.

Try saying:

We’re vaccinating today so your child will have the best protection possible long before the start of any kind of sexual activity.

We vaccinate people well before they are exposed to an infection, as is the case with measles and the other routinely recommended childhood vaccines.

Similarly, we want to vaccinate children long before they are exposed to HPV.

FAQ 3 (female): Is HPV important? If a woman gets regular PAP smears she won’t get cervical cancer.

Cervical cancer causes 4,000 deaths/ year in the U.S. with our current system of preventive screening

Among women with cervical cancer, 28% had normal PAP w/in 3 years of dxn
Preventing Cervical Cancer with Pap Smears Has Risks

- 330,000 women undergo cone/LEEP procedures every year
- LEEP/conization associated with obstetric morbidity
  - Preterm delivery
  - Preterm rupture of membranes
  - Low birth weight
  - Long term developmental outcomes, neonatal intensive care costs

**WHY REMOVE HALF THE CERVIX WHEN YOU COULD GET A SHOT IN THE ARM INSTEAD?**

FAQ 3 (male): *Is HPV important? My son won’t get cervical cancer so why bother with this?*

Average Number of New HPV-Associated Cancers by Sex, in the United States, 2005-2009

**Women (N=20,413)**
- Vagina: 4%
- Vulva: 15%
- Oropharynx: 11%
- Anus: 15%
- Cervix: 55%

**Men (N=12,002)**
- Vagina: 4%
- Vulva: 15%
- Oropharynx: 14%
- Anus: 8%
- Penis: 8%
- Cervix: 55%

Try saying:

*HPV vaccine is very important because it prevents cancer.*

*I want your child to be protected from cancer.*

*That’s why I’m recommending that your daughter/son receive the first dose of the HPV vaccine series today.*
FAQ 4: Isn’t the HPV vaccine too new to know if it works?

Summary of Effect to Date

- Vaccine is very effective at preventing infection with relevant types
  - Vaccinated people
  - “Herd” immunity
- Decreases in genital warts

FAQ 5: Is HPV vaccine safe?

HPV Vaccine Safety

- 57 million doses of HPV vaccine distributed in US from 2006 – 2013 (many more abroad)
- The most common adverse events reported were considered mild (e.g., sore arm)
- For serious adverse events reported, no unusual pattern or clustering that would suggest that the events were caused by the HPV vaccine
- These findings are similar to the safety reviews of MCV4 and Tdap vaccines

Moms in focus groups
- Stated concerns about both short- and long-term vaccine safety
- Not aware that HPV vaccine was tested
- Concerned that their child’s fertility could be affected by the vaccine
Post-Vaccination Syncope (PVS)

- Serious injuries have occurred from PVS
- ACIP recommends that “vaccine providers should strongly consider observing patients for 15 minutes after they are vaccinated. If syncope develops, patients should be observed until the symptoms resolve.”
- Among the 41 PVS reports with secondary injuries and info about the timing of syncope:
  - 76% occurred in adolescents aged 11 to 18 years
  - Time from vaccination to syncope onset was <5 minutes in 49%, <15 minutes in 80% of the reports
  - 10 of the 41 (24%) sustained injuries that were serious

Try saying:

This is not a new vaccine and for years HPV vaccine has been shown to be very effective and very safe.

HPV vaccine has a similar safety profile to the meningococcal and Tdap vaccines.

HPV vaccine has been very carefully studied by scientific experts and it’s safety is continually monitored.

Like other shots, side effects can happen, but most are mild and go away quickly, primarily arm pain or redness. HPV vaccine has not been associated with any long-term side effects.

FAQ 6: Will my child see this as “permission” to have sex?

Receipt of HPV vaccine does not increase sexual activity or decrease age of sexual debut

- Kaiser Permanente Center for Health Research
- 1,398 girls who were 11 or 12 in 2006, 30% of whom were vaccinated, followed through 2010
- No difference in markers of sexual activity, including
  - Pregnancies
  - Counseling on contraceptives
  - Testing for, or diagnoses of, sexually transmitted infections
Try saying:

Several research studies have shown that getting the HPV vaccine does not make kids more likely to be sexually active.

These studies have also shown that getting the HPV vaccine does not make kids more likely to start having sex a younger age.

FAQ 7: Would you give HPV vaccine to your child?

- Emphasizing your personal belief in the importance of HPV vaccine helps parents feel secure in their decision
- Some respondents in focus groups stated that they would feel more comfortable knowing that the doctor had vaccinated their own child or was planning to (if the child was <11)
- Respondents in an online survey stated that knowing that oncologists supported the recommendation made them more likely to get their child vaccinated

Try saying:

I have given HPV vaccine to my son/daughter (or grandchild/niece/nephew/friend’s children).

I strongly believe in the importance of this cancer-preventing vaccine.

Experts, such as the American Academy of Pediatrics, cancer doctors, and the CDC, also agree that getting the HPV vaccine is very important for your child.

Learning Objective #3

TIPS ON HAVING YOUR WHOLE OFFICE TEAM FEEL COMFORTABLE COMMUNICATING ABOUT HPV VACCINE
5 Communication Tips

1. Be sure that everyone who has patient contact gets educated on HPV vaccination.
2. Be sure that each office staff group knows their role in immunization communication.
3. Encourage questions; interpret them as natural caution, not refusal.
4. Remember to arrange for the next dose.
5. Remember to give the VIS with each dose.

For more information visit:

- CDC
- AAP
- Immunization Action Coalition
- CHOP Vaccine Education Center

Email questions or comments to CDC Vaccines for Preteens and Teens:
PreteenVaccines@cdc.gov

http://www.cdc.gov/vaccines/who/teens/for-hcp/tipsheet-hpv.html
Objectives of this Session

- Develop a strategy for improving delivery of HPV vaccine in a primary care setting
- Apply the Model for Improvement to test changes, using immunization-focused tools and resources
- Implement a measurement strategy to monitor changes made

Research vs. Quality Improvement

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Measurement for Research</th>
<th>Measurement for Learning and Process Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>To discover new knowledge</td>
<td>One large &quot;blind&quot; test</td>
<td>To bring new knowledge into daily practice</td>
</tr>
<tr>
<td>Tests</td>
<td>Many sequential, observable tests</td>
<td>Stabilize the biases from test to test</td>
</tr>
<tr>
<td>Biases</td>
<td>Control for as many biases as possible</td>
<td>Gather &quot;just enough&quot; data to learn</td>
</tr>
<tr>
<td>Data</td>
<td>Gather as much data as possible, &quot;just in case&quot;</td>
<td>and complete another cycle</td>
</tr>
<tr>
<td>Duration</td>
<td>Can take long periods of time to obtain results</td>
<td>&quot;Small tests of significant changes&quot; accelerates the rate of improvement</td>
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</tbody>
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It Takes an Effective Team to Do QI Work!

- Members representing different kinds of expertise in the practice
  - Clinical Leader
  - Technical Expertise
  - Day-to-Day Leadership
  - Administrative Staff
  - Parent Partner
  - Project Sponsor
Fundamental Questions for Improvement

- What are we trying to accomplish?
- How will we know that a change is an improvement?
- What changes can we make that will result in an improvement?

Model for Improvement

What are we trying to accomplish?

How will we know that a change is an improvement?

What change can we make that will result in improvement?

Act

Plan

Study

Do

AIM

MEASURES

IDEAS

Example (Poor)

- Our practice team will improve communication with parents who are hesitant about their adolescent receiving HPV vaccine.

Sample AIM Statement

By July 31, 2014, our practice team will improve immunization processes in our practice for adolescents so that:
- 95% of our patients seen for any type of visit will have their immunization status assessed.
- 95% of our patients will receive all vaccines for which they are eligible (based on ACIP recommendations) at a visit.
- 90% of our patients will receive appropriate immunizations reminders or recall notices.
- 90% of our patients will be UTD with all ACIP recommended immunizations, including 3 doses of HPV vaccine.
- 90% of our patients will have their current immunization information sent to the NIIS (electronically or manually entered) within 7 days of vaccine administration.
Model for Improvement

What are we trying to accomplish?

How will we know that a change is an improvement?

What change can we make that will result in improvement?

Act

Plan

Study

Do

How will we know a change is an improvement?

- Requires measurement
- Build measurement into daily work routine
  - Data should be easy to obtain and timely
  - Small samples over time
- Use qualitative & quantitative data
  - Qualitative data is highly informative
  - Qualitative data is easy to obtain

One practice’s immunization status measurements...

% of 3 doses HPV vaccine at 13-17 yrs. old
What Changes Can We Make That Will Result in Improvement?

Tests of Change need 2 components:
1. Change concepts (ideas): ready for use or ready to adapt to your unique environment.
2. PDSA test method

The PDSA Cycle for Learning and Improvement

Act
- What changes are to be made
- Next cycle?

Plan
- Objective
- Questions and predictions (why)
- Plan to carry out the cycle (who, what, where, when)
- Plan for data collection

Study
- Complete the analysis of the data
- Compare data to predictions
- Summarize what was learned

"Did it work?"

Do
- Carry out the plan
- Document problems and unexpected observations
- Begin analysis of the data

"Let's try it!"

Use of the PDSA Cycles

Multiple cycles

Changes that Result in Improvement

Evidence
Best Practice
Testable Ideas

Data

Very Small Scale Test

Follow-up Tests

Wide-Scale Tests of Change

Implementation of Change

Why Test?

- **Increase** your belief that the change will result in improvement
- **Opportunity** for learning from “failures” without impacting performance
- **Document** how much improvement can be expected from the change
- **Learn** how to adapt the change to conditions in the local environment
- **Evaluate** costs and side-effects of the change
- **Minimize** resistance upon implementation
Decrease the Time Frame for a PDSA Test Cycle

- Years
- Quarters
- Months
- Weeks
- Days
- Hours
- Minutes

Drop down next "two levels" to plan Test Cycle!

Overall Aim: Improving HPV Vaccination Rates (and Preventing Disease!)

Assess immunization status at every visit
Recommend HPV vaccine at age 11-12
Elicit patient/family questions and concerns
Conduct Reminders/Recalls

How teams get results

- Engage leaders
- Form team
- Assign responsibility for key tasks
- Meet
- Small tests of change
- Use of the NJIIS and/or decision-support in your EMR.
- Use of best practices, tools and resources

From Charles Darwin:

“It is not the strongest of the species that survive, nor the most intelligent, but the one most responsive to change.”