From Acquisition to Disease: 
HPV Epidemiology and 
Natural History

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UCLA School of Nursing
... were to build an HPV lesion...

- **Essential ingredients**
  - Basal membrane (giving rise to epithelial cells)
  - Differentiating epithelium
  - HPV
  - Exposure
    - trauma to allow penetration of virus to the lowest layer of the epithelium
Flattening of the epithelial cells, loss of the nucleus, ghost-like appearance at the outermost layer.
In addition...

- The cost of treating HPV infection-related dysplasias among women is high
  - Sexual revolution of the 1960’s and prevalence
- Incidence of HPV 16 infection
  - 4-5 cases/100 person years
- Current treatments
  - Ablative
    - Treat manifestations of infection
  - Cannot distinguish between “doomed” and the “spontaneous remitters”
The capsid is made from two late proteins: L1, L2

“Filled” with double-stranded DNA viral genome
Capsid peptides bind with cell surface receptors in basal cell layer

Alpha-7 integrin molecule is one of the candidate receptors (Frazer et al.)
Early proteins that regulate the virus are expressed in lowest layers of epithelium

Infection spreads laterally at first
Late proteins are expressed in upper layers of epithelium

Infection and consequent atypias begin to ascend
Scope of the Problem

- 20 million infected with HPV
- Common infection
  - 1,500,000 LSIL
- Significant associated mortality
  - 500,000 HSIL
- CA 4100

Significant associated mortality
Prevalence and Incidence of HPV Infection

- Approximately 20 million people are currently infected with HPV in the United States\(^1\)
- Annual incidence of sexually transmitted HPV infection is \(\sim 5.5\) million\(^1\)
- HPV incurs the highest direct medical costs of all STDs other than HIV, at $1.6 billion annually\(^2\)
- Overall, an estimated 75% of sexually active men and women have been exposed to HPV at some point in their lives\(^3\)

HPV = Human Papillomavirus; STDs = Sexually transmitted diseases.

### Common HPV Types Associated With Benign and Malignant Disease

<table>
<thead>
<tr>
<th>HPV Types</th>
<th>Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-Risk</strong></td>
<td>6, 11</td>
</tr>
<tr>
<td></td>
<td>Benign low-grade cervical changes</td>
</tr>
<tr>
<td></td>
<td>Condylomata acuminata (genital warts)</td>
</tr>
<tr>
<td><strong>High-Risk</strong></td>
<td>16, 18, 31, 33, 45</td>
</tr>
<tr>
<td></td>
<td>Low-grade cervical changes</td>
</tr>
<tr>
<td></td>
<td>High-grade cervical changes</td>
</tr>
<tr>
<td></td>
<td>Cervical cancer</td>
</tr>
<tr>
<td></td>
<td>Anogenital and other cancers</td>
</tr>
</tbody>
</table>

HPV Infection in the United States

- Genital warts
- Detected by colposcopy
- HPV DNA positive: Colposcopy negative
- Presence of antibodies (negative HPV test)
- Not currently infected

~75% of population exposed to HPV

Most Prevalent HPV Types That Cause Cervical Cancer

HPV DNA was detected in 1,739 of the 1,918 patients with cervical cancer.

HPV Infection in Young Women

HPV positive (percent)

<table>
<thead>
<tr>
<th>Lifetime number of sex partners</th>
<th>HPV positive (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>21</td>
</tr>
<tr>
<td>2-3</td>
<td>32</td>
</tr>
<tr>
<td>4-5</td>
<td>54</td>
</tr>
<tr>
<td>6-9</td>
<td>56</td>
</tr>
<tr>
<td>10+</td>
<td>69</td>
</tr>
</tbody>
</table>

HPV Infection Among College-Age Women


Predictive Factors for HPV Infections: College Women

- Smoking
- Oral Contraceptive Use
- Report of new male sexual partner
  - In particular, 1 known for <8 months
Epidemiology of Cervical Cancer

- Second most common cancer in women worldwide\(^1\)
  - Estimated 400,000-500,000 cases of cervical cancer diagnosed each year\(^2\)
  - Surpassed only by breast cancer, domestically & internationally

- In the United States, the estimated incidence is ~8.0/100,000\(^3\)
  - ~10,520 new cases and ~3,900 deaths annually\(^3\)
  - Even though >50 million Pap smears are performed each year\(^4\)
  - ~half of cervical cancer cases are attributable to one HPV Type

- Equal opportunity disease...
  - Half of the cases will occur in women never screened and an additional 10% in women not screened within the past 5 years\(^5\)

- Cost of US cervical cancer screening programs, using Pap test, >$5 billion annually\(^6\)

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Patterns for Pap testing and Undertreatment of Pap test Abnormalities within Ten Years of Diagnosis of Cervical Cancer; 1981

Proportion of Cervical Cancer Cases Diagnosed in 1981 Showing Undertreatment of Pap Test Abnormalities in Prior 10 years

Number of Women Eligible, Showing None, One or Two Prior Pap tests in Prior 10 Years
Swedish Registry in 1981

Age Group - Birth Cohorts in 1981

Number of Women

Total Number of Women
No prior Pap Test
1 Prior Pap test
2 Prior Pap tests
3 Prior Pap tests

% Women Screen > 1 time in 10 years

0 10000 20000 30000 40000 50000 60000
30-39 40-49 50-59 60-69 >70

Percent
0 20 40 60 80 100
Cervical Cancer is Not an Equal Opportunity Disease

Cervical Cancer is Not an Equal Opportunity Disease

Epidemiology of Genital Warts

- One of the most common STDs
- ~1.4 million (1%) individuals in the United States currently have genital warts
- Incidence of genital warts is underestimated
- Annually, 500,000-1,000,000 new cases of genital warts occur in the United States
- ~264,000 initial office visits for genital warts in the United States annually (NDTI)

NDTI = National Disease and Therapeutic Index 2003.
HMO data suggest EGWs disproportionately affect young men and women and peak at different ages for each...

Cervical Cancer Rates Have Plummeted Since the 1930s

- Nearly 70% reduction; attributable to Pap test screening
- Still, approximately 10,000-12,000 incident US cases annually
- Nearly 4,000 US women perish annually
- Almost all cervical cancers are due to HPVs
Transmission of HPV

• Intimate skin-to-skin contact with an infected partner is necessary for transmission\(^1\)
  – Intromissive intercourse is not strictly necessary\(^1,2\)
  – Men implicated in epidemiologic chain of the infection\(^3\)
• Incubation period ranges from weeks to several months\(^4\)
• Source contact usually has subclinical infection\(^5\)
• Perinatal transmission can, in rare instances, cause recurrent respiratory papillomatosis in infants and young children\(^6\)
• Condoms may not prevent HPV infection\(^7\)
  – Condom usage should be encouraged to decrease the risk of HIV and other STDs

Factors Associated With Higher Risk of HPV Infection

**Women**
- Age\(^1,2\)
- Sexual behavior\(^1,2\)
  - Increased risk associated with >number of male sexual partners\(^1,2,3\)
  - Risk increases with earlier age of first sexual intercourse\(^4\)
- Sexual history of the male partner\(^1,2\)
- Immunologic status\(^5\)
  - HPV more likely in immuno-suppressed women

**Men**
- Lifetime number of sexual partners\(^6\)
- Number of recent sexual partners\(^6\)
- Uncircumcised\(^6\)
- Same-sex encounters\(^7\)

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### Healthcare Costs of Cervical HPV

**Cost per episode of care** ($)

<table>
<thead>
<tr>
<th></th>
<th>Negative</th>
<th>ASC</th>
<th>Any abnormal</th>
<th>LSIL</th>
<th>AGC</th>
<th>HSIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visits (n)</td>
<td>1</td>
<td>2.6</td>
<td>3.5</td>
<td>4.5</td>
<td>5.1</td>
<td>6.9</td>
</tr>
<tr>
<td>Pap tests (n)</td>
<td>1</td>
<td>2.2</td>
<td>2.5</td>
<td>2.7</td>
<td>3.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Duration (months)</td>
<td>-</td>
<td>7.4</td>
<td>9.6</td>
<td>10.9</td>
<td>13.7</td>
<td>17.4</td>
</tr>
</tbody>
</table>

*Average age adjusted to the 1998 US female population; all cost estimates were converted to 2002 dollars. ASC = atypical squamous cells; AGC = atypical glandular cells; LSIL = low-grade squamous intraepithelial lesion; HSIL = high-grade squamous intraepithelial lesion.

Natural History of HPV Infection
Natural History of HPV Infection

Inoculation

Prophylactic vaccination

First lesion

Immune response

Host containment

Sustained clinical remission

Persistent or recurrent disease

Asymptomatic infection

Active growth

Late stage

Available at: http://www.arhp.org/healthcareproviders/onlinepublications/clinicalproceedings.cfm?ID=149
Natural History of HPV Infection (cont’d)

- Most individuals will get HPV at some time
- In most cases, HPV either clears or becomes undetectable
- Persistence of high-risk HPV can lead to true precancer


- Long persistence of HPV and CIN 3 are necessary for the accumulation of random mutations that lead to cancer
Natural History of Cervical Neoplasia

Typical Sequence of HPV-Related Events

- Menarche
- Sexual debut
- Oncogenic HPV infection
- CIN & HPV DNA +
- CIN 3/CIS & HPV DNA +
- CIS untreated & HPV DNA +
- Micro inv CxCA & HPV DNA +
- Inv CxCA & HPV DNA +

Concomitant accumulation of genetic "hits"

Years
Natural History of Cervical Neoplasia

Typical Sequence of HPV-Related Events

- Menarche
- Vaccination
- Sexual debut
- Oncogenic HPV infection
- CIN & HPV DNA +
- CIN 3/CIS & HPV DNA+
- CIS untreated & HPV DNA+
- Micro inv CxCA & HPV DNA+
- Inv CxCA & HPV DNA+
The Future of Prevention:
An Overview of HPV Vaccines
Impact of Routine Vaccination on Vaccine-Preventable Diseases in the US

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percent decrease</th>
<th>Number of reported cases</th>
<th>Maximum number of cases reported prior to introduction of vaccine</th>
<th>Reported cases in 2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>71.7%</td>
<td>26,612</td>
<td>7526</td>
<td></td>
</tr>
<tr>
<td>Hib</td>
<td>98.7%</td>
<td>20,000</td>
<td>259</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>99.9%</td>
<td>56</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Polio (Paralytic)</td>
<td>100%</td>
<td>16,316</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td>98.5%</td>
<td>1314</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td>92.1%</td>
<td>11,647</td>
<td>147,271</td>
<td></td>
</tr>
<tr>
<td>Diphtheria</td>
<td>99.9%</td>
<td>1</td>
<td>175,885</td>
<td></td>
</tr>
<tr>
<td>Small Pox</td>
<td>100%</td>
<td>48,164</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Rubella</td>
<td>99.9%</td>
<td>47,745</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Mumps</td>
<td>99.8%</td>
<td>152,209</td>
<td>231</td>
<td></td>
</tr>
</tbody>
</table>

Hib = *Haemophilus influenzae* type b

Vaccination Success Stories

1950
- Paralytic polio strikes 20,000 American; ~1900 associated deaths
- Measles vaccine licensed

1958-1962
- Half a million cases of measles each year; 432 measles-related deaths

1963
- Measles vaccine licensed

1985 and before
- ~20,000 children develop Hib every year; 600 annual deaths

1985
- Hib vaccine licensed

2003
- ~56 cases

2003
-~259 cases

Today

~259 cases

No reported cases
HPV Vaccine Trials
HPV, Cervical Cancer, and Vaccines

- Cervical cancer is a consequence of infection with human papillomavirus (HPV)
- Worldwide cervical cancer is a significant cause of death with >250,000 deaths/yr
- Clinical trials of subunit vaccines show promise for preventing HPV infection and sequelae

Courtesy of Dr Eliav Barr.
HPV 11 VLP Vaccine: Serologic Response

HPV 18 Serology/RIA Results


N = 37
Trial of an Experimental HPV 16 VLP Vaccine

2392 women (1533 evaluable), ages 16-23 years

Randomized

40mg/dose

HPV 16 VLP vaccine (N=768)

Intramuscular injections
- Day 0
- Month 2
- Month 6

Placebo (N=765)

225 µg aluminum adjuvant/dose

• Primary endpoint
  - Persistent HPV 16 infection, defined as the detection of HPV 16 DNA in samples obtained at 2 or more visits

• Secondary endpoint
  - Tolerability of vaccine

Efficacy Analysis of an HPV 16 VLP Vaccine

Incidence of AEs was similar in both groups; the most frequent adverse experience was pain at the injection site.

CIN = cervical intraepithelial neoplasia; PCR = polymerase chain reaction; AEs = adverse events

## Serious AEs in HPV 16 Study

<table>
<thead>
<tr>
<th>Serious adverse events</th>
<th>Vaccine group (n=1194)</th>
<th>Placebo group (n=1198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to vaccination</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>During study</td>
<td>4 (0.4%)</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Withdrawal from study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due to vaccine-related adverse event</td>
<td>3 (0.3%)</td>
<td>4 (0.3%)</td>
</tr>
<tr>
<td>Due to serious adverse event</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Clinical adverse events during the 14 days after any of the 3 vaccinations.

HPV 16 VLP as a Potential Vaccine: 4-Year Results

Vaccine was 94% effective

Reduction in CIN Following HPV Type 16 Vaccine

- 2391 women aged 16–23 years enrolled
  - 552 vaccinated
  - 544 given placebo
- Pap tests on day 0, month 7,12,18,24,30,36,42, and 48
- Magnitude of reduction in CIN lesions increased in lesion severity
- Observed efficacy
  - CIN 1 29.7%
  - CIN 2 42.6%
  - CIN 3 72.7%

Trial of a Bivalent L1 VLP Vaccine in Prevention of HPV 16/18 Infection

Every 6 months participants were tested for cervical HPV DNA, cytology, and serum antibody levels; every 3 months, participants were tested for HPV presence by PCR.

Vaccine group (n=560)
(20 mg HPV 16 L1; 20 mg HPV 18 L1)

Placebo group (n=553)
500 mg aluminum hydroxide

Endpoints

- Primary objective
  - Assess vaccine efficacy in the prevention of infection with HPV 16, HPV 18, or both

- Secondary objective
  - Evaluation of vaccine efficacy in the prevention of cytologically confirmed LSIL, HSIL, and histologically confirmed LSIL (CIN1), HSIL (CIN 2 or 3) squamous cell cancer, or adenocarcinoma

Randomized

1113 women 15-25 years of age

- No more than 6 sexual partners
- No history of an abnormal Pap test or ablative or excisional treatment of the cervix
- No ongoing treatment for external condylomata
- Cytologically negative, seronegative for HPV 16, HPV 18 and HPV negative for 14 high risk HPV types

HPV 16/18 Vaccine Efficacy

According-to-protocol analyses

- Persistent infection: 100% efficacy, P<0.0001
- Incident infection: 91.6% efficacy, P<0.007

Intention-to-treat analyses

- Persistent infection: 95.1% efficacy, P<0.0001
- Cytological abnormalities: 92.9% efficacy, P<0.0001

### Serious AEs in HPV 16/18 Study

<table>
<thead>
<tr>
<th>Serious adverse events</th>
<th>Vaccine group (n=531)</th>
<th>Placebo group (n=538)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to vaccination</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>During study*</td>
<td>22 (4.0%)</td>
<td>19 (3.5%)</td>
<td>0.636</td>
</tr>
<tr>
<td>Withdrawal from study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due to nonserious adverse event</td>
<td>0</td>
<td>3 (0.6%)</td>
<td>0.249</td>
</tr>
<tr>
<td>Due to serious adverse event</td>
<td>1 (0.1%)</td>
<td>0</td>
<td>0.497</td>
</tr>
</tbody>
</table>

*Participants who reported a serious adverse event during the entire study period (month 0-27).

Phase 2 Study of a Quadrivalent HPV Vaccine

Randomized

1115 women 16 to 23 years

≤5 lifetime sexual partners

Administered on
day 0, month 2,
and month 6

HPV 6, 11, 16, 18 Vaccine

Placebo

• Primary endpoint
  – Immunogenicity to the 4 HPV components at 7 months in individuals HPV naive at baseline

• Secondary endpoint
  – Establish appropriate dosing for Phase 3 trials

Vaccine was generally safe, well tolerated, and induced a massive humoral immune response

Geometric mean titers after the third dose of anti-HPV 6, 11, 16, 18 antibodies were 43-, 46-, 140-, and 29-fold higher in immunized women than in those with previous infection and were not dose dependent

A Phase 3 trial for this quadrivalent vaccine designed to evaluate the safety, immunogenicity, and efficacy is currently underway

Phase 3 Study of Quadrivalent HPV Vaccine: FUTURE II Study

17,800 women, 19 to 23 years

Vaccine group
HPV 6, 11, 16, 18

Placebo

Endpoints
- Efficacy
- Immunogenicity
- Safety

Intramuscular injections at 0, 2, 6 months

Randomized

5 years

FUTURE = The Females United to Unilaterally Reduce Endo-ectocervical Disease
Available at: http://www-cme.erep.uab.edu/onlineCourses/uab_insight/summer03/cervical_cancer/ID0152.htm
Potential Benefits of HPV Vaccine

- Historically, vaccines have represented a cost-effective means to prevent disease induced by microbial agents and other pathogens.
- Potential reduction in incidence of
  - Cervical cancer and its precursor lesions
  - Other associated cancers (anal, penile, vaginal, vulvar)
  - Genital warts

Immunization Against HPV

- Epidemiologic studies suggest type-specific immunity
- Type-specific neutralizing antibodies
- Excellent vaccine candidate
  - Virus-like particles (VLP) are recombinant viral capsids that induce type-specific neutralizing antibody in animal models
- VLP vaccines are nontoxic and immunogenic in humans
- Phase 2 trials completed; Phase 3 trials with HPV 16/18 and/or HPV 6/11 VLP vaccine are now underway

Incidence of Cervical Dysplasia in Adolescents

- Adolescents are at high risk for high-grade lesions
- Retrospective review of adolescents ≤18 years old
  - Median age in LSIL cohort (n=477) was 16.7
    - 199 (47.2%) had ASC-US, LSIL, or CIN 1
    - 77 (18.2%) had HSIL, CIN 2, CIN 3, or AIS
    - 146 (34.6%) had negative follow-up
  - Median age in HSIL cohort (n=55) was 16.9
    - 15 (27.3%) had ASC-US, LSIL, or CIN 1
    - 28 (50.9%) had HSIL, CIN 2, CIN 3, or AIS
    - 12 (21.8%) had negative follow-up

Are Women Ready for a Cervical Cancer Vaccine?

Study objectives

- Evaluate willingness to accept a vaccine for themselves and their children (8—14)
- Determine what factors play a role in their decision making
- Respondents were stratified by ethnicity, household income, marital status, and education level

Are Women Ready for a Cervical Cancer Vaccine? (cont’d)

• Results
  – 74% willing to vaccinate themselves
  – 69% who had a daughter and 64% who had a son would consent to have their child vaccinated

• Reasons given not to vaccinate
  – Unknown side effects
  – Believe that minors are sexually inactive
  – No direct benefit of vaccinating males

Overcoming Barriers to Vaccine Acceptance
Scope of the Problem

- Common infection: 20 million infected with HPV
- 1,500,000 LSIL
- 500,000 HSIL
- CA 4100

Significant associated mortality
Cervical Cancer is Not an Equal Opportunity Disease

Cervical Cancer Rates Have Plummeted Since the 1930s

- Nearly 70% reduction; attributable to Pap test screening
- Still, approximately 12,000 incident US cases annually
- Nearly 4000 US women perish annually
- Almost all cervical cancers are due to HPVs
There Are Obvious Benefits of Vaccines to Prevent HPV Infections
Advantages of HPV Vaccination

The development and use of a vaccine for HPV prevention has the potential to

- Decrease morbidity and mortality worldwide
  - Nearly half-million women diagnosed with malignancy annually
    - One-quarter million women die annually
- Alleviate emotional suffering
- Economic impact
  - Cancer-prevention activities
  - Cancer treatment
  - “Years” of life lost
Given These Obvious Benefits of HPV Vaccination

Why are there questions about vaccine acceptance?
Levels of Intervention

HPV Vaccine Acceptance

- Vaccine Developed
  - Systems: Research
- Vaccine Available
  - Systems and Communities: Payers and providers
- Vaccine Accepted?
  - Disease Incidence Decreased
  - Individuals' Behaviors Influenced by Systems, Communities
- Individual Issues
- Cultural Issues
- Family/Parent Issues
- Provider Issues

Individuals' behaviors are influenced by systems, communities, and families/parents. The process of vaccine acceptance is complex and involves various factors such as vaccine development, availability, and cultural issues. The disease incidence decreases as vaccine acceptance increases.
Extended Parallel Process Model

Fear

Perceived Threat

Perceived Susceptibility
Risk of experiencing a health threat

Perceived Severity
Beliefs about the significance or magnitude of the threat, including social consequences
“How effective might this intervention be in preventing the feared outcome?”

“How effective might I be in actually ‘achieving’ the recommended intervention?”
Barriers to Vaccine Acceptance

Individual and Family Issues
Barriers to Vaccine Acceptance
Individual and Family Issues: Lessons From HBV Vaccine Research

- Poor knowledge about Hepatitis B vaccines
  - 25% of clinic providers think adolescents lack knowledge
    - Caused, rather than prevented, disease
    - Serious side effects associated with vaccine
  - Only 47% of adolescents could correctly convey any correct information about vaccinations
    - 27% stated they knew nothing
    - 20% gave incorrect information
    - Only 20% of adolescents could correctly define a vaccination
  - No difference between groups previously vaccinated for HBV and those not

Barriers to Vaccine Acceptance
Lessons from HBV Vaccine Research

• Specific barriers to vaccination can be identified consistently by providers and adolescents alike
  – 94% of clinic providers: “adolescents don’t like getting shots”
    • Developmental norms
    • Idea of systems vs individual decision-making approach
  – 50% suggested “time constraints” were a barrier

Mrs. Smith, now that your daughter is 11, it's time for her to get vaccinated for HPV, a sexually transmitted infection.
I HATE shots!
She wants to go to the mall on Saturday…Susie’s best friend just pierced her naval…what is it with those bare midriffs…you want me to argue with her to come to the clinic 3 times for 3 shots in how many months…?
Factors Affecting the Rate of Immunization Exemptions Among School-Age Children...

- Approximately 30% reduction of exemptions associated with number and type of procedures required to obtain an exemption
  - Dose response
- Administrative procedures required to obtain an exemption
  - Required annual renewal of exemption
  - Letter from parents for religious exemption
  - Signature of religious leader, school official, physician
  - Written information informing parents requesting exemption of the risks associated with nonparticipation

Barriers to Vaccine Acceptance

Lessons from HBV Vaccine research

• Specific barriers to vaccination can be identified consistently by providers and adolescents alike
  – Surprisingly...
    • 56% of providers “little perceived threat”
    • 43% of providers “poor efficacy of the vaccine”

Barriers to HPV Vaccine Acceptance

Individual and Family Issues

- Poorly informed public
  - Many have not heard of HPV; for some, “disease” is the first knowledge
  - Link of HPV to Pap testing is not widely understood
  - Poor understanding of Pap testing results

- Information desired by women
  - What is HPV?
  - How do you get HPV?
  - How can HPV be prevented?
  - Information should be given before initiation of sexual activity of HPV

- Source of information
  - Those whose source was a doctor had greater knowledge of HPV
  - Doctors identified as a preferred source of information on HPV
Barriers to Vaccine Acceptance
Individual Issues: Attitudes Toward Vaccination

• Will desire for information translate into vaccine acceptance?
  – Stigma related to STI
  – Vaccine acceptance as acknowledgement of risky behavior

• Can we reframe the discussion to the relevant issue?
  – Describing HPV vaccines as a vaccine to prevent cervical cancer
Ms. Smith, I’d like you to get vaccinated against HPV, a very common infection, but one that can cause cancer or genital warts.
Barriers to Vaccine Acceptance

Individual Issues: Research on Acceptability

- Small qualitative and quantitative studies suggest high levels of interest
  - Parents, young adults, adolescents
    - Nearly three-quarters of respondents in each study group suggested they would view vaccines positively

- The key determinants of intention to get vaccinated
  - Sexual transmission as mode is not a barrier
  - Recommendation by a provider is important
  - Cancer prevention is compelling
    - Prevention of warts may be more compelling for youth
  - Warts prevention may ↑ acceptability

Kahn et al. (2003), Boehner et al. (2003), Mays et al. (2004), Davis et al. (2004), Zimet et al. (2005)
Barriers to Vaccine Acceptance

Parental Issues
Barriers to Vaccine Acceptance

Parental Issues: Consent and Concerns

• Parental consent likely to be required
  – For some period of time after availability
  – Most adolescents look to their parents for healthcare decisions

• Potential parental concerns
  – Sexual nature of transmission
    • Approval of vaccine = approval of sex
    • Vaccination → early initiation of sex/reduced condom use
  – How to describe the vaccine to adolescent or preadolescent child
Barriers to Vaccine Acceptance

Provider Issues
How am I going to talk with Mrs. Smith and her 11 year old daughter about this new vaccine?
Barriers to Vaccine Acceptance

Provider Issues

- Parents look to healthcare providers for guidance...but
  - Will providers be willing to recommend HPV vaccine?
  - Will providers be comfortable recommending vaccination?
  - Do providers have the skills to talk about this kind of vaccine with parents and children?

- Potential concerns for healthcare providers
  - STI issue and communication
  - Anticipation of angry parent
  - Parents with antivaccination beliefs
  - How to describe the vaccine to adolescent or preadolescent child
Barriers to Vaccine Acceptance
Provider Issues: Research

- 2 studies
  - Positive disposition toward recommending STI vaccination
  - Mays et al. (2004) - study of pediatric nurse practitioners’ willingness to recommend STI vaccines to parents of adolescents
  - Raley et al. (2004) - study of obstetricians’ and gynecologists’ willingness to recommend HPV vaccines for adolescents

- What are the key determinants of willingness to recommend vaccination?
  - Approval of professional organization (AAP and ACOG)
  - Older age of patient
  - Relative reluctance to vaccinate 11- to 13-year-olds
Barriers to Vaccine Acceptance

Summary

• Studies of individuals, parents, and providers all show
  – High levels of interest in an HPV vaccine for children
  – Parents are motivated by desire to protect their children
  – Parents and providers show a relative reluctance around vaccination of younger vs older adolescents
Barriers to Vaccine Acceptance

Other Issues to Consider

• Communicating risks associated with HPV infection
  – Infection is common but usually clears spontaneously
  – Warts are typically benign from a medical viewpoint
    • Stigmatizing and often of great concern
  – Cervical cancer is rare, but very serious
  – The communication challenge is to emphasize the severity of persistent high-risk HPV infection as a cause of cancer, while not invoking confusion, guilt, or psychological stress

• Anticipation of dissemination of information and misinformation regarding HPV and HPV vaccination
  – Internet information
  – Press coverage
Overcoming the Barriers

• Research is reassuring
  – Young women and parents of adolescents want to know more about HPV
  – Women desire and value information from healthcare providers
  – The majority of women and parents feel very positively about HPV vaccination for themselves and their children
  – For most, the STI issue is not a significant obstacle
  – Parents and patients look to their healthcare providers for vaccine recommendations

• Important to anticipate some opposition
  – From those who are broadly antivaccine
  – From those who have specific concerns about vaccination or preventive strategy for any STI
Warning: This vaccine may not protect you against HPV Types 1-5, 31, 33, 35, 52, 56, cp6108, is39, ....
Overcoming the Barriers
Specific Recommendations

• Initiate conversation about parental concerns or questions about vaccines, generally, and about HPV vaccine, specifically
  – Be respectful even if parents’ opinions are based on misinformation
    • Respectful discussion is more likely to result in a positive outcome
  – Written information of risks for not participating
    • Corrective information can be delivered during the interview, via written material, and through provision of websites
  – Empowered parents
    • Shared decision-making

• Comprehensive approach
  – Belief that education about vaccine should be part of comprehensive education
    • Pap tests, DNA testing, and other behavioral issues relevant to women’s health
  – Realize what can be done in the time you have with each parent and patient
  – We don’t need to repeat the mistakes of prior campaigns for vaccination of preadolescents, adolescents, and young adults
Overcoming the Barriers

Broader Recommendations

• Clinician education
  – Clinicians
    • Benefits of the vaccine
    • Focus on the herd, not the individual
      – Picking out who will be at risk
  – Develop terminology and a lexicon
  – Utilitarian vs sexuality and morality: “part of what we do at the 10- or 11-year-old’s visit”
  – Sensitivity to societal concerns about sexual activity in adolescents
Overcoming the Barriers
Broader Recommendations

- Public health initiatives
  - Clinicians need to see themselves as policymakers
  - Policymakers need to see themselves as stakeholders
  - Endorsement by major health provider societies and advocacy groups
  - National leaders should be convinced of the value of vaccination
  - Acceptance could be gained by emphasizing the anticancer aspects of the vaccine, but the STD component, including genital warts, cannot be ignored