HPV vaccine perspectives

Dr. David Prado Cohrs
Universidad Francisco Marroquín, Guatemala
President of the Sexually Transmitted Diseases Committee, SLIPE
Disclosure statement

• The presenter has received honoraria from Novartis and GlaxoSmithKline (GSK) as an investigator in vaccine clinical trials, from GSK, Schering Plough and Aventis as an investigator in clinical antibiotics trials, from GSK as member of advisory boards and from Novartis and GSK as lecturer
• Overview of HPV
• HPV vaccines
• Why vaccinate at age 11 or 12 years?
• Safety of vaccines
• Strategies for increasing uptake
• Conclusions
• Overview of HPV

• HPV vaccines

• Why vaccinate at age 11 or 12 years?

• Safety of vaccines

• Strategies for increasing uptake

• Conclusions
Human papillomavirus

- HPV is a small virus containing circular double-stranded DNA within a spherical shell (capsid)

HPV is the most frequent sexually transmitted disease
• The cumulative risk of acquiring cervical HPV infection in women with only one sexual partner is **46%** (3 years after first sexual encounter)

• HPV infections are very common: up to 80% of women will acquire an HPV infection in their lifetime

HPV is the necessary cause of cervical cancer
Second human carcinogen (after tobacco)

→ 5% of cancer in humans

→ 10% of cancer in women

→ 15% of cancer in women in developing countries
It is also a cause of disease and death in developed countries.
HPV types

• At least 30 HPV types target the genital mucosa

• At least 15 HPV types are classified as oncogenic (high risk)

• Globally, HPV types 16 and 18 together account for > 70% of cervical cancer cases

HPV types

• Low-risk (non-oncogenic) types cause benign genital warts/lesions

• HPV type 6 is most commonly detected in genital warts (~90% of warts) followed by HPV type 11 (10–30% of warts)

HPV transmission

• Sexual intercourse and/or genital skin-to-skin contact are the primary routes (condom does not provide complete protection)

• Transmission by non-sexual routes is thought to be uncommon, but possible

Screening identifies existing pre-cancerous lesions
Vaccination prevents them occurring in the first place

Healthy

Pre-cancer

Cancer

Debilitation/death

Primary prevention

Secondary prevention

Treatment
One of the paradoxes of HPV is that clinicians who are largely responsible for vaccinating against cervical cancer, are unlikely to ever see a case of cervical cancer.
I think we are blind. Blind people who can see, but do not see

José Saramago
• Overview of HPV

• **HPV vaccines**

• Why vaccinate at age 11 or 12 years?

• Safety of vaccines

• Strategies for increasing uptake

• Conclusions
HPV vaccines: virus-like particles (VLP)

- VLPs consist of only one protein (L1)
- VLPs are virus particles without DNA hence are not infectious
- VLPs are immunologically identical to infectious virus

L1 protein → 360 copies → spontaneous assembly
No DNA inside (can not produce infection)
Antigen

Specificity of the immune response

Adjuvant system

Designed to enhance and modulate the immune response by combining the effect of two or more adjuvants

Composition of HPV2 and HPV4

**Cervarix®**

- **Antigens**
  - HPV 16 VLPs
  - HPV 18 VLPs
- **AS04 adjuvant**
  - Aluminium salt (Al(OH)_3)
  - MPL
- **AS04-containing vaccine**

**Gardasil®**

- **Antigens**
  - HPV 16 VLPs
  - HPV 18 VLPs
  - HPV 6 VLPs
  - HPV 11 VLPs
- **Adjuvant**
  - Aluminium salt (amorphous aluminium hydroxyphosphate sulphate [AAHS])
- **AAHS-containing vaccine**

MPL = monophosphoryl lipid A.

Gardasil is a registered trademark of MSD.
Advantages of Gardasil® over Cervarix®
• The Mercks’ quadrivalent vaccine also includes HPV 6 and 11 (non oncogenic types)

• Gardasil® has the advantage of protecting against genital warts

• Gardasil® is licensed for males
Advantages of Cervarix\textsuperscript{R} over Gardasil\textsuperscript{R}
• Cervarix$^R$ offers the advantage of a better cross-protection profile
Likely impact on cervical cancer

- Increased protection by 6 -- 12%
- Estimated protection from cervical cancer: 76 -- 82%
ACIP recommendations

• Females (either HPV 2 or HPV 4)
  – Routine: aged 11 to 12
  – Catch-up: aged 13 through 26 years

• Males (HPV 4)
  – Routine: aged 11 to 12
  – Catch-up: aged 13 through 21 (22 through 26 may be vaccinated)
ACIP recommendations

• Both vaccines are given as a 3-dose series
• The series can be started beginning at age 9 years
• Administer the 2\textsuperscript{nd} dose 1-2 months after the 1\textsuperscript{st} dose
• Administer the 3\textsuperscript{rd} dose 6 months after the 1\textsuperscript{st} dose
- Overview of HPV
- HPV vaccines
- **Why vaccinate at age 11 or 12 years?**
- Safety of vaccines
- Strategies for increasing uptake
- Conclusions
Initial HPV infection occurs soon after onset of sexual activity
<table>
<thead>
<tr>
<th></th>
<th>HPV DNA prevalence after sexual initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24 months</td>
</tr>
<tr>
<td><strong>Denmark</strong></td>
<td></td>
</tr>
<tr>
<td>(S.K. Kjaer et al. 2001)</td>
<td>35.4 %</td>
</tr>
<tr>
<td><strong>USA</strong></td>
<td></td>
</tr>
<tr>
<td>(L.Koutsky 2003)</td>
<td>40.0 %</td>
</tr>
</tbody>
</table>
NETWORK STRUCTURE LINKING 573 SECONDARY SCHOOL STUDENTS IN A ROMANTIC OR SEXUAL RELATIONSHIP WITH ANOTHER STUDENT AT "JEFFERSON HIGH", USA

Numbers in the graph represent occasions in which the pattern was observed (i.e., 63 individuals reported monogamous dyadic relationships)

Reproduced from: Bearman PS, Moody J, Stovel K. Am J Sociol 2004;110(1):44-91. Copyright 2004 by the University of Chicago, all rights reserved, with permission from the University of Chicago Press.
Infection is not harmless
HPV infection frequently results in dysplasia

- A cohort of 60 adolescent women (aged 14–17 years) was followed over a 2.2-year period
- HPV was detected in 45.3% of all specimens (HR types 38.6%, LR 19.6%)
- During the study period, 49 of 60 subjects tested positive for HPV (cumulative prevalence, 81.7%).
- 37% had at least 1 abnormal test (including 2% HGSIL)

Antibody response is optimal
Efficacy of vaccines is ideal
Vaccination does not modify sexual behavior
Cost-effectiveness is more favorable
Remember...

Women continue to be at risk for cervical cancer throughout their lives
Women might benefit from vaccination including women with previous HPV exposure
• Overview of HPV

• HPV vaccines

• Why vaccinate at age 11 or 12 years?

• Safety of vaccines

• Strategies for increasing uptake

• Conclusions
How do we know they are safe?

• Large clinical trials

• Over 120 million doses have been distributed globally, no serious safety concerns

• WHO’s Global Advisory Committee on Vaccine Safety concluded that both Cervarix® and Gardasil® had good safety profiles

WHO. *Wkly Epidemiol Rec* 2009; 84:117–132; Health Service Executive, Ireland; Laura Naranjo personal communication
• Safety experience in the UK: most reports have related either to the signs and symptoms of recognised, minor side effects listed in the product information, or to the injection process and not the vaccine itself (ie, psychogenic in nature)
Bachmann claims HPV vaccine might cause ‘mental retardation’

By Rachel Weiner, Published: September 13
Beam me up, Scotty!

There's NO intelligent life down here!
We all have one

USE IT
• Overview of HPV
• HPV vaccines
• Why vaccinate at age 11 or 12 years?
• Safety of vaccines
• Strategies for increasing uptake
• Conclusions
Communicating effectively with parents and patients

• Include HPV vaccines in discussion of all vaccines recommended in adolescents

• Use a short, matter-of-fact approach to HPV vaccine recommendation

• Emphasize cancer prevention

Strategies for increasing vaccine uptake

• The strongest predictor of a person being vaccinated is a physician recommendation

• Educate yourself to educate parents and patients about vaccines

• Address parents’ questions

• Immunize at every opportunity
• Overview of HPV
• HPV vaccines
• Why vaccinate at age 11 or 12 years?
• Safety of vaccines
• Strategies for increasing uptake
• Conclusions
• «HPV vaccines can prevent cancer in an entire generation»
• At least, 70% of cervical cancers could be prevented by HPV vaccines

Cervical cancer prevention: HPV vaccination combined with screening

Vaccination offers an important new management option in the primary prevention of cervical cancer

HPV vaccination combined with screening is the most effective cervical cancer prevention strategy

Vaccines in the time of HPV, represent a light of hope, so...

...the races condemned to one hundred years of solitude will have, at last and forever, a second opportunity on earth