# HPV Vaccine

# Issues for Consideration in the Updated Statement

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Advisory Committee on Immunization Practices
June 19, 2013

# Updated ACIP Statement

- **Updated information including:**
  - **Background information**
    - Burden of infection and cancers
    - Cervical cancer screening
  - **HPV vaccine data**
    - Bivalent and quadrivalent trial data
    - Duration of protection
    - Immunogenicity among HIV –infected persons
  - **HPV vaccine safety data**
    - Post-licensure data
  - **Impact and cost effectiveness**

# Updated ACIP Statement (2)

- **Pregnancy**
  - No wording changes for vaccine recommendations
  - Removal of quadrivalent vaccine in pregnancy registry reporting, continue to report to VAERS and Merck
- **Special populations**
  - Child sexual abuse – recommendation to start vaccination at age 9

# Updated ACIP Statement (3)

- **Special populations**
  - Immunocompromised persons – updates in information, harmonization of male and female language
  - End stage renal disease - consider addition of vaccination of males through age 26 years
  - Information about:
    - Select health care workers
    - Research HPV laboratory workers

# Immunocompromised persons

- **HIV-infected**
  - 1 clinical trial in men (Wilkins), 2 in women (Kahn, Money), 2 in children (Levin, Weinberg) demonstrated acceptable safety profile and immune response to vaccine
  - Some studies found differences in geometric mean titers compared to historic controls (Kahn, Levin); unclear if this finding has clinical significance
- **Other populations: ongoing evaluations**
- **Propose including these updates in the revised statement**

Wilkin T, et al. JID 2010; Levin MJ, et al. JAIDS 2010; Kahn J, et al. CID 2013.;Weinberg A, et al. JID 2012; Money, et al. CAHR 2013 Abstract.

# Recommended vaccinations indicated for adults based on medical and other indications

| VACCINE ▼ INDICATION ► | Pregnancy | Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) | HIV infection CD4+ T lymphocyte count: < 200 cells/μL | HIV infection CD4+ T lymphocyte count: ≥ 200 cells/μL | Men who have sex with men (MSM) | Heart disease, chronic lung disease, chronic alcoholism | Asplenia (including elective splenectomy and persistent complement component deficiencies) | Chronic liver disease | Kidney failure, end-stage renal disease, receipt of hemodialysis | Diabetes | Healthcare personnel |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Influenza [1,*] | 1 dose IIV annually | | | | | 1 dose IIV annually | | | | | |
| Tetanus, diphtheria, pertussis (Td/Tdap) [4,*] | 1 dose Tdap each pregnancy | Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs | | | | | | | | | |
| Varicella [5,*] | Contraindicated | | | 2 doses | | | | | | | |
| Human papillomavirus (HPV) Female [6,*] | | 3 doses through age 26 yrs | | | | 3 doses through age 26 yrs | | | | | |
| Human papillomavirus (HPV) Male [7,*] | | 3 doses through age 26 yrs | | | | 3 doses through age 21 yrs | | | | | |
| Zoster [8] | Contraindicated | | | | 1 dose | | | | | | |
| Measles, mumps, rubella (MMR) [9,*] | Contraindicated | | | 1 or 2 doses | | | | | | | |
| Pneumococcal polysaccharide (PPSV23) [8,] | | | | | | 1 or 2 doses | | | | | |
| Pneumococcal 13-valent conjugate (PCV13) [10] | | | | | | 1 dose | | | | | |
| Meningococcal [11,*] | | | | | 1 or more doses | | | | | | |
| Hepatitis A [12,*] | | | | | | 2 doses | | | | | |
| Hepatitis B [13,*] | | | | | | 3 doses | | | | | |

*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

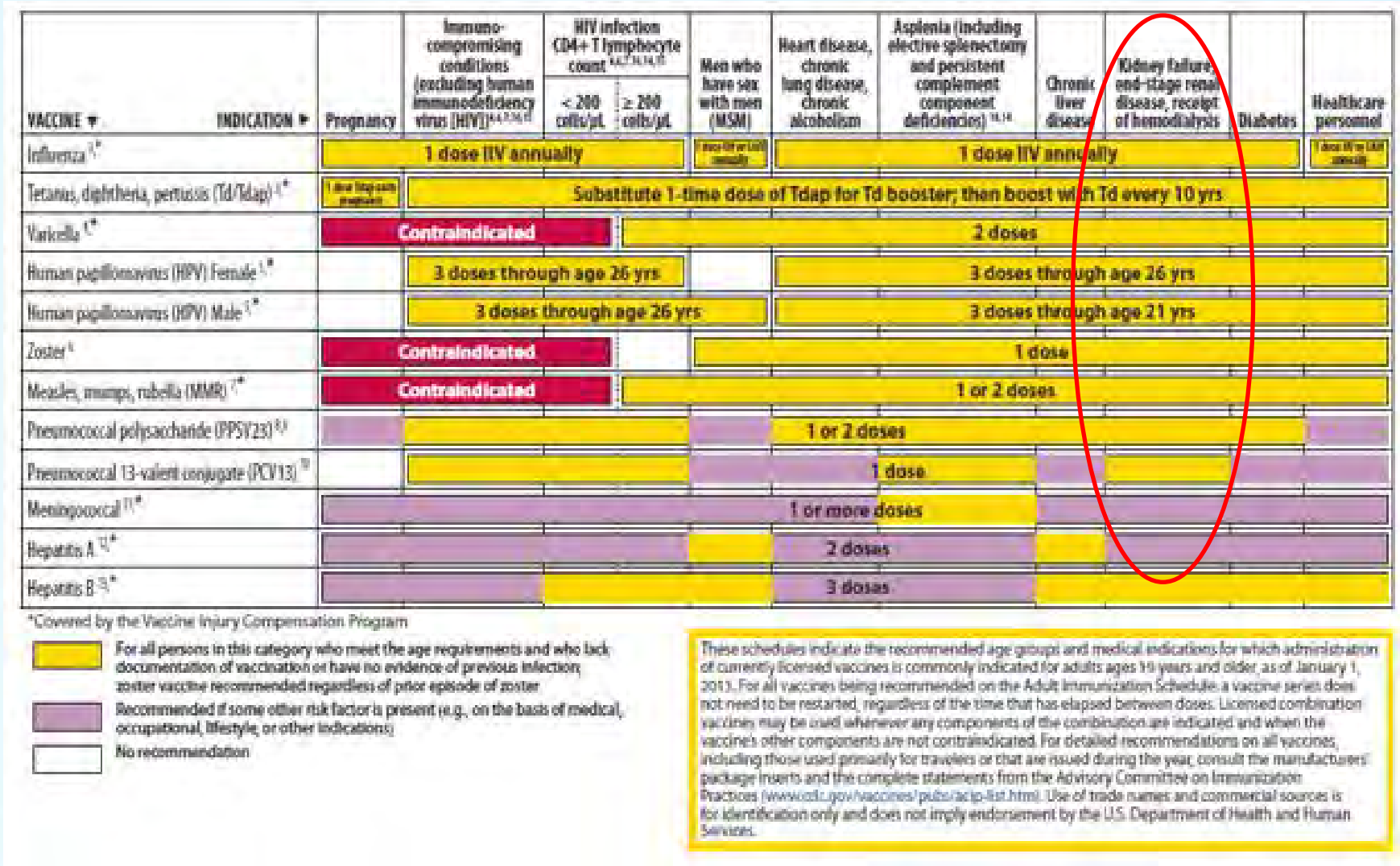
Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

These schedules indicate the recommended age groups and medical indications for which administration of currently licensed vaccines is commonly indicated for adults ages 19 years and older, as of January 1, 2013. For all vaccines being recommended on the Adult Immunization Schedule, a vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Licensed combination vaccines may be used whenever any components of the combination are indicated and when the vaccine's other components are not contraindicated. For detailed recommendations on all vaccines, including those used primarily for travelers or that are issued during the year, consult the manufacturers' package inserts and the complete statements from the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/pubs/acip-list.html). Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

http://www.cdc.gov/vaccines/schedules/hcp/adult.html

# Recommended vaccinations indicated for adults based on medical and other indications



| VACCINE ▼ INDICATION ▶ | Pregnancy | Immunocompromising conditions (excluding human immunodeficiency virus [HIV])[4,6,7,16,17] | HIV infection CD4+ T lymphocyte count[4,6,7,14,17] < 200 cells/μL | HIV infection CD4+ T lymphocyte count[4,6,7,14,17] ≥ 200 cells/μL | Men who have sex with men (MSM) | Heart disease, chronic lung disease, chronic alcoholism | Asplenia (including elective splenectomy and persistent complement component deficiencies)[16,18] | Chronic liver disease | Kidney failure, end-stage renal disease, receipt of hemodialysis | Diabetes | Healthcare personnel |
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# Kidney failure, end-stage renal disease (ESRD), receipt of hemodialysis

- **Propose extending vaccination for males through age 26 years: Why?**
  - Data suggest higher burden of HPV-associated lesions including anogenital warts, cervical dysplasia in persons with ESRD as well as post renal transplant
    - Primarily descriptive data
    - No data on vaccine immunogenicity or efficacy in-this group
    - Quadrivalent HPV vaccine licensed through age 26 years for males
  - Many with ESRD and age <26 years will receive renal transplant

Banerjee S, et al. Indian J Dermatol Venereol Leprol. 2007; Leight IM, et al. Rec Reslts Cancer Res. 1995; Euvard S, et al. Cancer. 1993; Fairley CK, et al. Nephrol Dial Transplant 1994; Haberal AN, et al. Diagn Cytopathol. 2008

# Research HPV laboratory workers and select healthcare workers

- Is there a risk to research HPV laboratory workers of acquiring HPV from work with wild type virions and newer synthesized virions ("quasi virions")?
- Is there a risk to select healthcare (HC) workers of acquiring HPV (secondary to surgical smoke)?
  - Issue also considered in STD Treatment Guidelines Meeting April, 2013

# Background: laboratory

- Human Papillomavirus is difficult to culture – this is why PCR for DNA is used to evaluate for infection
- However, some research laboratories are working with wild type HPV as well as newer synthesized virions to characterize natural history and immunity to HPV
- 6 + laboratories in the US conducting research in which laboratory generated virions are being produced
  - e.g. NIH, UNM, Penn State, Iowa, Wisconsin, UAB

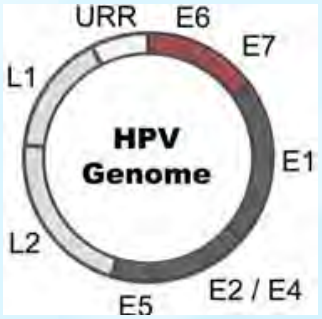
# Virions used in the laboratory

- Wild type HPV
  - Infected xenografts grown in immunocompromised animals or transfected keratinocytes grown in organotypic raft cultures
  - Generation of these infectious virions is time-consuming and produces relatively low virus yields
- Newer laboratory techniques have allowed development of laboratory-generated virions: "pseudo virions" or "quasi virions"
  - "Pseudo virions" have a reporter gene; no oncogenes and not believed to be infectious
  - "Quasi virions" are laboratory-generated virions synthesized in the 293TT cell system; they consist of papillomavirus (PV) L1 and L2 enclosing complete ~8 Kb PV genomes
  - "Quasi virions" are generally indistinguishable from tissue-derived PV (wild type) virions

McCance Proc.Natl Acad Sci.1988; Meyers C J Virol. 1997;Pyeon et al. Proc Natl Acad Sci. 2005;
Culp TD J Virol. 2006

# “Quasi virion”


+




Transfect

293 TT cells

48 hours

Lyse cells and mature Quasivirion for 24hrs

CsCl gradient

# Potential risk of HPV acquisition?

- Wild type virions and "quasi virions" are infectious
  - Papillomas were produced when "quasi virions" injected in the skin of rabbits
  - These virions contain whole HPV genomes including oncogenes and other elements associated with disease/cancer development
  - Synthesis of "quasi virions" produces high titers (up to $10^9$ transducing units from a single 75-$cm^2$ flask of cells)
  - Minimal infectious dose not known

# Potential exposures in the laboratory?

- Cutaneous or mucosal (environmental surfaces with virion)
- Respiratory (aerosolization of virion by vortexing or other procedures)

- High virion titers of "quasi virions" but potential risk not characterized
  - No evidence of previous exposure/infection/disease in laboratory
  - Evidence in animal models (rabbit) in which exposure to "quasi virions" resulted in papillomas at site of inoculation

# Summary: research HPV laboratory workers

- Potential risk of HPV acquisition to research HPV laboratory workers working with wild type and "quasi virions"
- Limited data on risk and no data on transmission or vaccine efficacy in this setting

- Propose language for inclusion in the updated ACIP statement

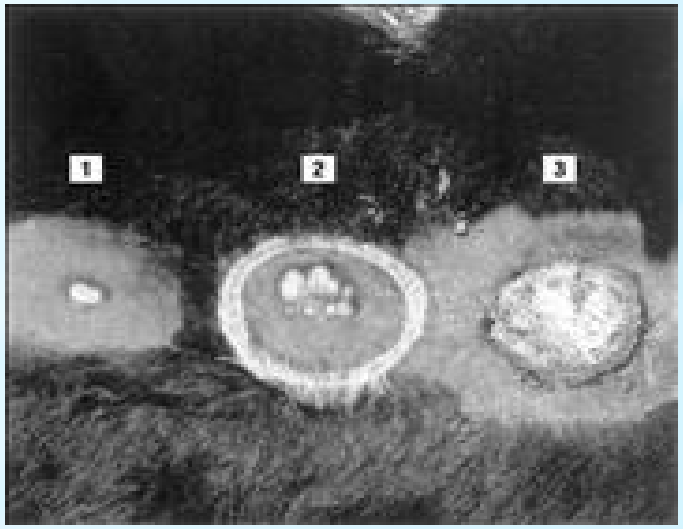
# Is there a risk to healthcare workers of acquiring HPV during treatment of anogenital lesions(secondary to surgical smoke)?

- Seven studies of CO2 laser for warts and 1 study of electrocautery (LEEP) for CIN demonstrated HPV DNA in the smoke plume after therapy
- Evidence exists from bovine papillomavirus models that virions in smoke plume are infectious
- 2 case reports of laryngeal papillomas reported in health care workers who treated anogenital warts
  - Unclear if RRP was a result of this potential exposure

Garden. Arch Dermatol.2002; Garden JAMA. 1988; Andre J,et al. Am Acad Dermatol. 1990; Hallmo, et al. Eur Arch Otorhinolaryngol 1991; Calero, et al. Laryngorhinootologie. 2003; Kashima, et al. Otolaryngol Head Neck Surg. 1991; Ferenczy, et al. Obstet Gynecol. 1990; Sawchuk J Am Acad Dermatol. 1989; Sood,et al. Infect Dis Obstet Gynecol. 1994; Weyandt , et al. Arch Dermatol Res. 2011

# Bovine models

- Smoke plume suctioned, collected and re-inoculated into skin of calves
  - Plume samples all + for bovine papillomavirus
  - All calves developed fibropapillomas at site of inoculation




Garden. Arch Dermatol. 2002.

# Infection control: current recommendations

- Local exhaust ventilation (e.g. smoke evacuator) is recommended when CO2 laser or electrosurgical procedures are performed on patients with angenital warts or anogenital tract intraepithelial neoplasia*

CDC-National Institute for Occupational Safety and Health. Control of Smoke form Laser/Electric Surgical Procedures. NIOSH Publication Number 96-128, available at http://www.cdc.gov/niosh/docs/hazardcontrol/hc11.html, Accessed 4/17/2013.

# Summary: select healthcare workers

- Smoke plumes generated by electrocautery and laser CO2 can contain papillomavirus
- Current recommendations include use of a smoke evacuator for these procedures
- Although two case reports in literature, unclear if the potential exposure led to the disease (RRP)
- Limited data on risk and vaccine efficacy in this setting

- Proposed language for inclusion in the updated ACIP statement

# Draft Language

- Research HPV laboratory and select healthcare workers might have an increased risk of acquiring HPV from occupational exposures. These persons include those working in laboratories and handling wild type virus or "quasi virions", and healthcare workers treating anogenital intraepithelial neoplasias or anogenital warts with laser CO2 or electrocautery.
- In the laboratory setting, proper infection control should be instituted including at minimum BSL2.
- Healthcare workers treating anogenital intraepithelial neoplasias or anogenital warts with laser CO2 or electrocautery should have vacuum ventilation as recommended by NIOSH.
- The need for any additional infection control steps in these settings is being investigated. It is unclear if there would be a benefit of HPV vaccination in these settings as there are no data on transmission risk or vaccine efficacy.

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- ACIP HPV Workgroup

# Thank you

**For more information please contact Centers for Disease Control and Prevention**

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