



VIRGINIA EPIDEMIOLOGY BULLETIN

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Human Papillomavirus (HPV)

This article summarizes the recommendations by the Advisory Committee on Immunization Practices (ACIP) for the use of quadrivalent human papillomavirus (HPV) vaccine [MMWR: March 23, 2007/56; 1-24]. It includes discussions on the epidemiology of HPV, describes the licensed HPV vaccine, and provides recommendations for vaccine use. The complete report can be accessed at www.cdc.gov/vaccines/pubs/ACIP-list.htm.

Introduction

Genital human papillomavirus is the most common sexually transmitted infection in the United States; an estimated 6.2 million persons are newly infected every year. Although the majority of infections cause no symptoms and are self-limited, persistent genital HPV infection can cause cervical cancer in women and other types of anogenital cancers and genital warts in both men and women.

On June 8, 2006, a quadrivalent HPV vaccine (Gardasil®, manufactured by Merck and Co., Inc.) was licensed for use among females aged 9-26 years for prevention of cervical cancer, cervical cancer precursors, vaginal and vulvar cancer precursors, and anogenital warts caused by HPV types 6, 11, 16, and 18.

Biology and Pathogenesis

Human papillomaviruses are small, nonenveloped, double-stranded DNA viruses in the family Papillomaviridae. Isolates of HPV are classified as “types”; more than 100 HPV types have been identified. Types are designated on the basis of the nucleotide sequence of the outer capsid protein L1. Most HPV types infect the cutaneous epithelium and cause common skin warts. About 40 types infect the mucosal epithelium; these are categorized according to their epidemiologic association with skin cancer. Infection with low-risk, non-oncogenic types can cause benign or low-grade cervical cell abnormalities, genital warts, and laryngeal papillomas. High-risk, oncogenic types can cause low-grade cervical cell abnormalities, high-grade cervical cell abnormalities that are precursors to cancer, and anogenital cancers. High-risk HPV types

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are detected in 99% of cervical cancers. Type 16 is the cause of approximately 50% of cervical cancers worldwide, and types 16 and 18 together account for about 70% of cervical cancers. Although infection with a high-risk HPV type is considered necessary for the development of cervical cancer, by itself it is not sufficient to cause cancer because the vast majority of women with HPV infection do not develop cancer. In addition to cervical cancer, HPV infection is also associated with less common anogenital cancers such as cancer of the vulva, vagina, penis, and anus.

HPV infections occur at the basal epithelium and are thus largely shielded from the host immune response. Humoral and cellular immune responses have been documented, but correlates of immunity have not been established. Serum antibodies against many different viral products have been demonstrated. However, not all infected persons have antibodies; in one study, 54%-69% of women with incident HPV 6, 16, or 18 had antibodies. Among newly infected women, the median time to seroconversion is approximately eight months.

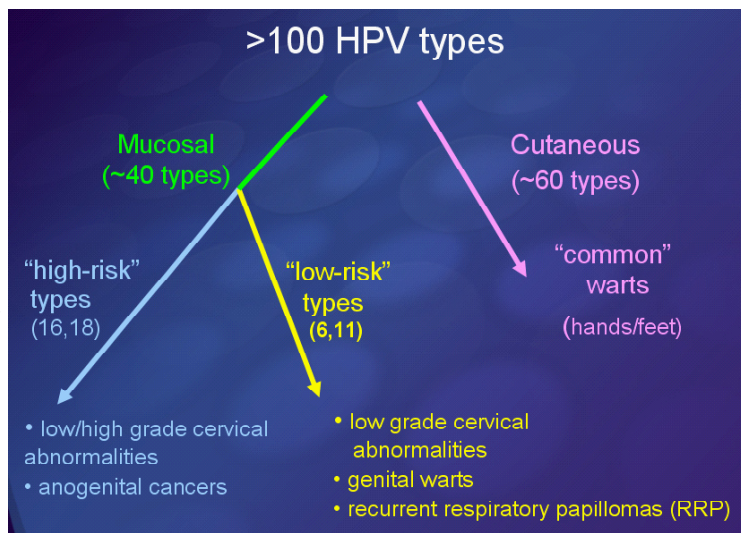
Although the incidence of infection is high, most infections are asymptomatic and resolve spontaneously; 70% of new HPV infections clear within one year. A small proportion of infected persons become persistently infected. Persistent infection with high-risk HPV types is the most important risk factor for the development of cervical cancer precursor lesions, with HPV 16 being more oncogenic than other high-risk HPV

types. The most common clinically significant manifestation of persistent genital HPV infection is cervical intraepithelial neoplasia, or CIN. Within a few years of infection, low-grade CIN (CIN 1) may develop, which may spontaneously resolve and the infection clear. Persistent HPV infection, however, may progress directly to high-grade CIN (CIN2 or CIN3). High-grade abnormalities are at risk of progression to cancer and so are considered cancer precursors. A small proportion of high-grade abnormalities spontaneously regress. If left undetected and untreated, years or decades later CIN2 or CIN3 can progress to cervical cancer.

Infection with one type of HPV does not prevent infection with another type. Of persons infected with mucosal HPV, 5% to 30% are infected with multiple types of the virus.

Laboratory Diagnosis

HPV has not been isolated in culture. Infection is identified by detection of HPV DNA from clinical samples. Assays differ considerably in their sensitivity and type specificity, and detection is also affected by the anatomic region sampled as well as the method of specimen collection.



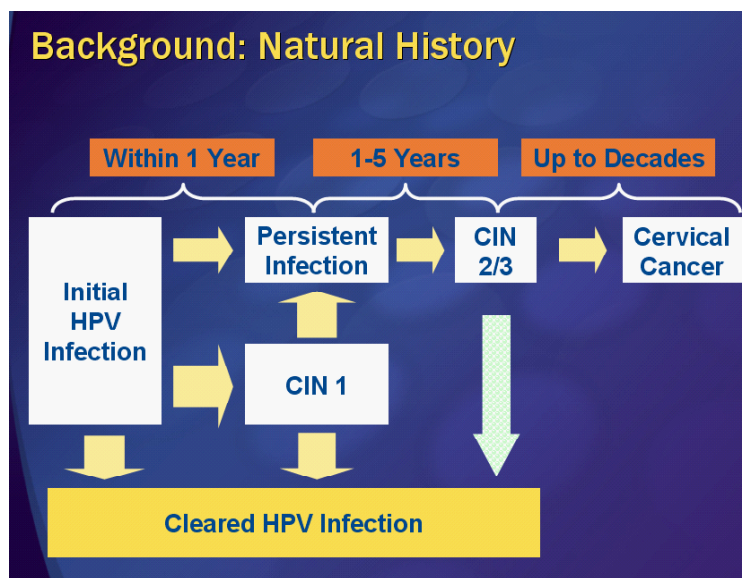
13 high-risk types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68). Results are reported as positive or negative and are not type-specific. The HC2 test is approved for triage of women with equivocal Papanicolaou (Pap) test results (atypical cells of undetermined significance) and in combination with the Pap test for cervical cancer screening in women over age 30. The test is not clinically indicated nor approved for use in men.

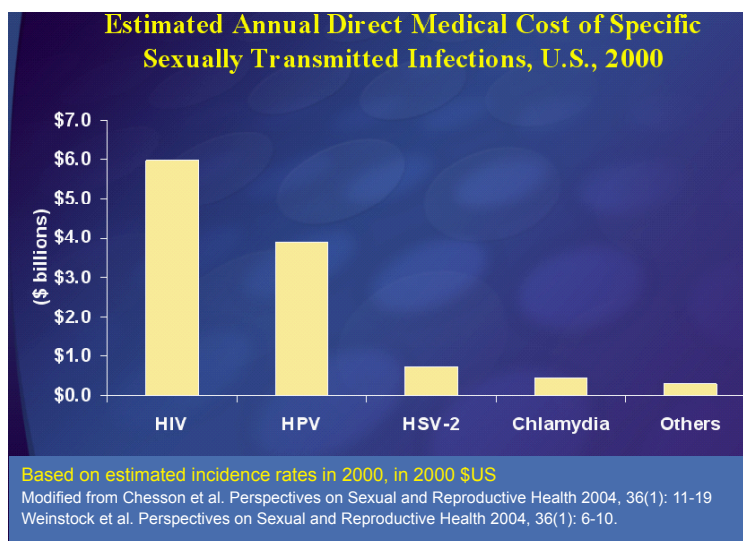
Epidemiologic and basic research studies of HPV generally use nucleic acid amplification methods that generate type specific results. HPV serologic assays, generally enzyme immunoassays (EIAs), exist. However, laboratory reagents used for these assays are not standardized and there are no standards for setting a threshold for a positive result.

Epidemiology of HPV Infection

Transmission and Risk Factors

Genital HPV infection is primarily transmitted by genital contact, usually through sexual intercourse. In virtually all studies of HPV prevalence and incidence, the most consistent predictors of infection have been measures of sexual activity, most importantly the number of sex partners (lifetime and recent). For example, one study indicated that 14.3% of women aged 18-25 years with one lifetime sex partner, 22.3% with two lifetime sex partners, and 31.5% with more than three lifetime partners had HPV infection. Most studies also sug-





gest that young age (less than 25 years) is also a risk factor for infection.

Transmission of HPV through other types of genital contact in the absence of penetrative intercourse has been described, but is less common. Genital HPV infection also can be transmitted by nonsexual routes, such as transmission from a mother to a newborn baby, but this is rare.

HPV is presumably communicable during both the acute infection and during persistent infection. However, this issue is difficult to study because of the inability to culture the virus. Communicability is presumed to be high because of the large number of new infections estimated to occur each year.

Studies of newly acquired HPV infection demonstrate that infection occurs soon after onset of sexual activity. In a prospective study of college women, the cumulative incidence of infection was 40% by 24 months after first sexual intercourse. Of all HPV types, HPV 16 acquisition was highest and accounted for 10.4% of infections; 5.6% had acquired HPV 18.

Because HPV is transmitted by sexual activity, understanding the epidemiology of HPV requires data on sexual behavior. The 2002 National Survey of Family Growth indicated that 24% of females in the United States were sexually active by age 15 years. This percentage increased to 40% by age 16 years and to 70% by age 18 years. Among sexually active females aged 15-19 years and 20-24 years, the median number of lifetime male sex partners was 1.4 and

2.8, respectively. The 2005 Youth Behavioral Risk Survey indicated that 3.7% of female students had been sexually active before age 13 years. Of those sexually active, 5.7% of 9th-grade females and 20.2% of 12th-grade females had had four or more sex partners.

Disease Burden in the United States

An estimated 20 million persons are currently infected with HPV, and an estimated 6.2 million new HPV infections occur annually. HPV infection is common among adolescents and young adults. Prevalence among adolescent girls is as high as 64%. Up to 75% of new infections occur among persons 15-24 years of age. Modeling estimates suggest that more than 80% of sexually active women will have been infected by age 50 years. HPV infection is also common in men. Among heterosexual men in clinic-based studies, prevalence of genital HPV infection is often greater than 20%. Prevalence is highly dependent on the anatomic sites sampled and method of specimen collection.

The two most common types of cervical cancer worldwide, squamous cell carcinoma followed by adenocarcinoma, are both caused by HPV. The American Cancer Society estimates that in 2006 about 9,700 new cases of cervical cancer were diagnosed in the United States with approximately 3,700 deaths in women as a result of cervical cancer. HPV is believed to be responsible for nearly all cases of cervical cancer. HPV types 16 and 18 are associated with 70% of these cancers. In addition to cervical cancer, HPV is believed to be responsible for 90% of anal cancers, 40% of vulvar, vaginal, or penile cancers, and 12% of oral and pharyngeal cancers.

All anogenital warts are caused by HPV, and approximately 90% are associated with HPV types 6 and 11.

Routine reporting of anogenital warts (or of HPV) does not exist in the United States. Information on prevalence and incidence has been obtained primarily from clinic-based populations, such as family planning and sexually transmitted disease or university health clinic patients. These evaluations indicate that about 1% of the sexually active adolescent and adult population in the United States have clinically apparent genital warts.

About four billion dollars are spent annually on the management of sequelae of HPV infections, primarily for the management of abnormal cervical cytology and treatment of cervical neoplasia. This exceeds the economic burden of any other sexually transmitted infection except human immunodeficiency virus.

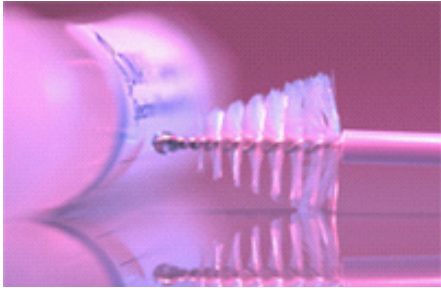
Treatment and Prevention of HPV Infection

There is no specific treatment for HPV infection. Medical management depends on treatment of the specific clinical manifestation of the infection. Treatment options for genital warts and cervical, vaginal, and vulvar cancer precursors include various local approaches that remove the lesion (e.g., cryotherapy, electrocautery, laser therapy, and surgical excision). Genital warts also are treated with topical pharmacologic agents. On the basis of limited existing data, available therapies for HPV-related lesions might reduce but probably do not eliminate communicability.

HPV transmission can be reduced, but not eliminated, with the use of physical barriers such as condoms. A study among newly sexually active college women demonstrated a 70% reduction in HPV infection when their partners used condoms consistently and correctly. For those who choose to be sexually active, a monogamous relationship with an uninfected partner is the strategy most likely to prevent future genital HPV infections. Abstaining from sexual activity (i.e., refraining from any genital contact with another person) is the surest way to prevent genital HPV infection.

Neither routine surveillance for HPV infection nor partner notification is useful for HPV prevention. Genital

HPV infection is so prevalent that the majority of partners of persons found to have HPV infection are infected already; no specific prevention or treatment strategies have been recommended for partners.



Cervical Cancer Screening

The majority of cervical cancer cases and deaths can be prevented through detection of pre-cancerous changes in the cervix by cytology using the Pap test. Currently available Pap test screening can be done by a conventional Pap or a liquid-based cytology. The American College of Obstetricians and Gynecologists (ACOG), the American Cancer Society (ACS), and the U.S. Preventive Services Task Force (USPSTF) guidelines state that all women should have a Pap test for cervical cancer screening within three years of beginning sexual activity or by age 21 years, whichever occurs first. While the USPSTF recommends a conventional Pap test at least every three years regardless of age, ACS and ACOG recommend annual or biennial screening of women younger than age 30 depending on use of conventional or liquid-based cytology, respectively. According to these national organizations, women over age 30 with three normal consecutive Pap tests should be screened every 2-3 years.

An estimated 82% of women in the United States have had a Pap test during the preceding three years. Pap test rates for all age and ethnic populations have increased during the preceding two decades. However, certain groups continue to have lower screening rates. These include women with less than a high school education (77%); foreign-born women, especially women who have been in the United States for <10 years (61%); women without health insurance (62%); and certain racial/ethnic

populations such as Hispanics (77%) and Asians (71%). Approximately half of women who had cervical cancer diagnosed in the United States had not had a Pap test in the three years before diagnosis.

The use of HPV vaccine does not eliminate the need for continued Pap test screening, since 30% of cervical cancers are caused by HPV types not included in the vaccine.

Quadrivalent Human Papillomavirus Vaccine

Composition

The currently licensed vaccine is a quadrivalent HPV vaccine (Gardasil®, Merck). The L1 major capsid protein of HPV is the antigen used for HPV vaccination. Using recombinant DNA technology, the L1 protein is expressed in *Saccharomyces cerevisiae* (yeast), and the proteins self-assemble into conformationally intact, noninfectious virus-like particles (VLPs) which are adsorbed on a 225 µg alum adjuvant. Each 0.5-mL dose contains 20 µg HPV 6 L1 protein, 40 µg HPV 11 L1 protein, 40 µg HPV 16 L1 protein, and 20 µg HPV 18 L1 protein. The formulation also includes sodium chloride, L-histidine, polysorbate 80, sodium borate, and water for injection. The quadrivalent HPV vaccine contains no thimerosal or antibiotics. It is supplied in single-dose vials and syringes.

Immunogenicity and Vaccine Efficacy

The immunogenicity of the quadrivalent HPV vaccine has been measured by detection of IgG antibody to the HPV L1 by a type-specific immunoassay developed by the manufacturer. In all studies conducted to date more than 99.5% of participants developed an antibody response to all four HPV types in the vaccine one month after completing the three-dose series. At that time interval, antibody titers against HPV types 6, 11,

16, and 18 were higher than those that developed after natural HPV infection.

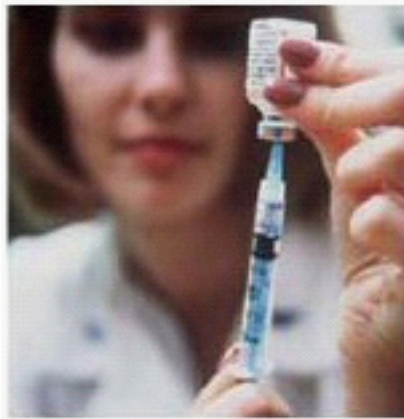
There is no known serologic correlative of immunity and no known minimal titer determined to be protective. The high efficacy found in the clinical trials to date has precluded identification of a minimum protective antibody titer. Further follow-up of vaccinated cohorts may allow determination of serologic correlates of immunity in the future.

HPV vaccine has been found to have high efficacy for prevention of HPV vaccine type-related persistent infection, and vaccine type-related CIN, CIN2/3, and external genital lesions in women 16–26 years of age. Clinical efficacy against cervical disease was determined in two double-blind, placebo-controlled trials, using various endpoints. Vaccine

efficacy was 100% for prevention of HPV 16 or 18-related CIN 2/3 or adenocarcinoma *in-situ* (AIS). Efficacy against any CIN due to HPV 6, 11, 16, or 18 was 95%. Efficacy against HPV 6, 11, 16, or 18-related genital warts was 99%.

Although high efficacy among females without evidence of infection with vaccine HPV types was demonstrated in clinical trials, there was no evidence of efficacy against disease caused by vaccine types with which participants were infected at the time of vaccination. Participants infected with one or more vaccine HPV types prior to vaccination were protected against disease caused by the other vaccine types, and prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types.

There is no evidence that the vaccine protects against disease due to non-vaccine HPV types or provides a therapeutic effect against cervical disease or genital warts present at the time of vaccination. A subset of participants in the phase II HPV vaccine study has been followed for 60 months post-dose one with no evidence of waning protection. Study populations will continue to



be followed for any evidence of waning immunity.

HPV vaccine has been shown to be immunogenic and safe in males. However, no clinical efficacy data are available for males. These studies are in progress.

Safety and Adverse Events

The quadrivalent HPV vaccine was evaluated for injection-site and systemic adverse events, new medical conditions reported during the follow-up period, and safety during pregnancy and lactation. Safety data on quadrivalent HPV vaccine are available from seven clinical trials and include 11,778 persons aged 9–26 years who received quadrivalent vaccine and 9,686 who received placebo. Detailed data were collected using vaccination report cards for 14 days following each injection of study vaccine on a subset of participants aged 9–23 years. The population with detailed safety data included 5,088 females who received quadrivalent HPV vaccine and 3,790 who received placebo.

In the study population with detailed safety data, a larger proportion of persons reported injection-site adverse events in the group that received quadrivalent HPV vaccine compared with aluminum-containing or saline placebo groups. Pain was the most common injection site adverse event, reported by 83.9% of vaccinees, 75.4% of those who received aluminum-containing placebo, and 48.6% of those who received saline placebo. Swelling and erythema were the next most common reactions in the vaccine and placebo groups. The majority of injection-site adverse experiences reported among recipients of quadrivalent HPV vaccine were mild to moderate in intensity; only 2.8%, 2.0%, and 0.9% of vaccinees reported severe pain, swelling, or erythema, respectively.

Systemic clinical adverse events, including nausea, dizziness, myalgia, and malaise were reported by a similar proportion of vaccine and placebo recipients in the population with detailed safety data. In both quadrivalent HPV vaccine and placebo groups, more persons reported a systemic clinical adverse experience in the 15 days after dose one compared with after dose two and after dose three. For the majority of

persons, the maximum intensity rating of systemic clinical adverse events was mild or moderate. Overall, 4.0%–4.9% of females who received quadrivalent HPV vaccine reported a temperature of $>100^{\circ}\text{F}$ ($>38^{\circ}\text{C}$) after dose one, two, or three.

Vaccine-related serious adverse events occurred in $<0.1\%$ of persons. The proportions of persons reporting a serious adverse event were similar in the vaccine and placebo groups, as were the types of serious adverse events reported. Seven persons had events that were determined to be possibly, probably, or definitely related to the vaccine or placebo. Five events occurred among quadrivalent HPV vaccine recipients and two among placebo recipients. The five events in the quadrivalent HPV vaccine group included bronchospasm, gastroenteritis, headache/hypertension, vaginal hemorrhage, and injection site pain/movement impairment.

In the overall safety evaluation, 10 persons in the group that received quadrivalent HPV vaccine and seven persons in the placebo group died during the course of the trials. None of the deaths were considered to be vaccine related.

Recommendations for Use of HPV Vaccine

Vaccination Schedule and Use

Quadrivalent HPV vaccine is licensed by the Food and Drug Administration for use among females 9–26 years of age. The recommended age for routine vaccination in the United States is 11–12 years. The vaccine can be given as young as nine years of age at the discretion of the clinician. The vaccine should be given at the same visit as other vaccines recommended for persons of this age (e.g., Tdap, meningococcal conjugate, hepatitis B).

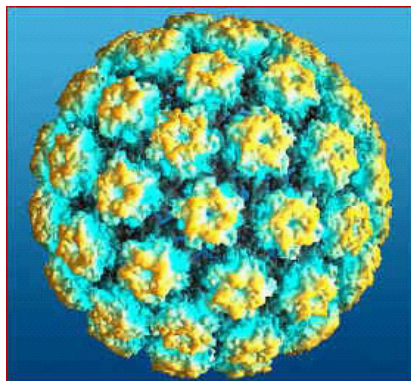
At the beginning of a vaccination program, there will be females older than 12 years of age who did not have the opportunity to receive vaccine at

age 11–12 years. Catch-up vaccination is recommended for females 13 through 26 years of age who have not been previously vaccinated or who have not completed the full series. Ideally, vaccine should be administered before potential exposure to HPV through sexual contact; however, females who may have already been exposed to HPV should be vaccinated. Sexually active females who have not been infected with any of the HPV vaccine types will receive full benefit from vaccination. Vaccination will provide less benefit to females if they have already been infected with one or more of the four HPV vaccine types. However, it is not possible for a clinician to assess the extent to which sexually active females would benefit from vaccination, and the risk of HPV infection may continue as long as persons are sexually active. Pap testing or screening for HPV DNA or HPV antibody is not a prerequisite for receiving HPV vaccination.

HPV vaccine is administered in a three-dose series by intramuscular injection. The second and third doses should be administered two and six months after the first dose. The minimum interval between the first and second doses is four weeks. The minimum interval between the second and third dose of vaccine

is 12 weeks. Doses administered at an interval shorter than the minimum interval should not be counted as valid and should be repeated. If the HPV vaccine schedule is interrupted, the vaccine series does not need to be restarted. If the series is interrupted after the first dose, the second dose should be given as soon as possible, and the second and third doses should be separated by an interval of at least 12 weeks. If only the third dose is delayed, it should be administered as soon as possible.

Although no data are available yet on administration of quadrivalent HPV vaccine with vaccines other than hepatitis B vaccine, the vaccine contains only HPV capsid protein and has no components that have been found to



adversely affect safety or efficacy of other vaccinations. The vaccine can be administered at the same visit as other age-appropriate vaccines, such as Tdap and quadrivalent meningococcal conjugate (MCV4) vaccines. Administering all indicated vaccines at a single visit increases the likelihood that adolescents and young adults will receive each of the vaccines on schedule. Each vaccine should be administered using a separate syringe at a different anatomic site.

HPV vaccine is not approved or recommended for females younger than nine years or older than 26 years of age. Studies with females older than 26 years of age are ongoing. There are no current studies among children younger than nine years of age.

Quadrivalent HPV vaccine is not licensed for use among males, and off-label use among males is not recommended.

Females who have an equivocal or abnormal Pap test could be infected with any of more than 40 high-risk or low-risk genital HPV types. It is unlikely that such females would be infected with all four HPV vaccine types, and they may not be infected with any HPV vaccine type. Therefore, women in the recommended age group with a previously abnormal Pap test may be vaccinated. Women should be advised that data do not indicate the vaccine will have any therapeutic effect on existing HPV infection or cervical lesions.

Females who have a positive HPV DNA test (Hybrid Capture 2®) done in conjunction with a Pap test could be infected with any of 13 high-risk types. This assay does not identify specific HPV types, and testing for specific HPV types is not done routinely in clinical practice. Women in the recommended age group with a positive HPV DNA test may be vaccinated. HPV DNA testing is not a prerequisite for vaccination. Women should be advised that the vaccine will not have a therapeutic effect on existing HPV infection or cervical lesions.

Clinically evident genital warts, or a history of genital warts, indicates infection with HPV, most often type 6 or 11. However, these females may be infected with HPV types other

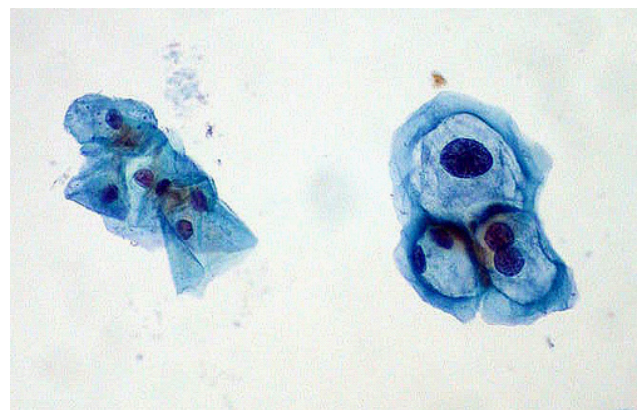
than the vaccine types, and therefore they may receive HPV vaccine if they are in the recommended age group. Women with a history of genital warts should be advised that data do not indicate the vaccine will have any therapeutic effect on existing HPV infection or genital warts.

Because quadrivalent HPV vaccine is a subunit vaccine, it can be administered to females who are immunosuppressed because of disease or medications. However, the immune response and vaccine efficacy might be less than that in persons who are immunocompetent. Women who are breastfeeding may receive HPV vaccine.

Contraindications and Precautions to Vaccination

A severe allergic reaction (acute respiratory distress or collapse) to a vaccine component or following a prior dose of HPV vaccine is a contraindication to receipt of HPV vaccine. A moderate or severe acute illness is a precaution to vaccination, and vaccination should be deferred until symptoms of the acute illness improve. A minor acute illness (e.g., diarrhea or mild upper respiratory tract infection, with or without fever) is not a reason to defer vaccination.

HPV vaccine is not recommended for use during pregnancy. The vaccine has not been associated with adverse outcomes of pregnancy or with adverse effects on the developing fetus. However, data on vaccination during pregnancy are limited. Until further information is available, initiation of the vaccine series should be delayed until after completion of the pregnancy. If a woman is found to be pregnant after initiating the vaccination series, the



ThinPrep liquid-based Pap. Normal squamous cells on left; HPV-infected cells with mild dysplasia (LSIL) on right.

remainder of the three dose regimen should be delayed until after completion of the pregnancy. If a vaccine dose has been administered during pregnancy, no intervention is indicated. A vaccine in pregnancy registry has been established; patients and healthcare professionals are urged to report any exposure to quadrivalent HPV vaccine during pregnancy by calling (800) 986-8999.

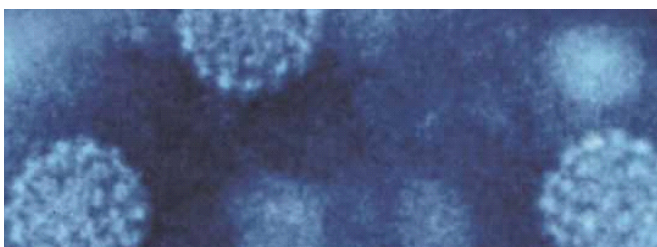
Conclusions

Anogenital HPV infection is believed to be the most common sexually transmitted infection in the United States. While most HPV infections are asymptomatic and result in no clinical disease, sequelae can include anogenital warts, recurrent respiratory papillomatosis, cervical cancer precursors, and cancers, including cervical, anal, vaginal, vulvar, penile, and some head and neck cancer. Since there is no specific treatment for HPV infection, efforts to reduce disease burden have largely been directed at screening for high-risk lesions. The availability of an effective preventive vaccine provides another tool for significantly reducing the risk of this pathogen.

Additional information on HPV for patients and healthcare professionals is also available from the CDC (www.cdc.gov/vaccines/vpd-vac/hpv/default.htm#patient).

References
MMWR: March 23, 2007/56; 1-24

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Division of Disease Prevention Pilots Partner Counseling and Referral Services Promotion

The VDH Division of Disease Prevention, in collaboration with the Arlington and Alexandria Health Districts and community-based organizations, is pilot-testing promotion of partner counseling and referral services (PCRS) for sexually transmitted infections. PCRS, also called partner notification or contact tracing, is an effective method of identifying new cases of disease and interrupting disease transmission. The process, however, is sometimes looked upon with suspicion by clients, making it difficult to obtain partner names from reluctant citizens.



Highlighting the anonymity of the process, the Division seeks to promote PCRS as a service provided for clients rather than just a routine health department activity. Marketed as “Disclosure Assistance Services”, the campaign includes a set of nine postcards featuring personal vignettes about the benefits of using Disclosure Assistance Services, four posters, a pamphlet, and a web page. All materials are available in English and Spanish. Materials will be distributed in health department clinics, through community-based outreach, and physicians’ practices. The program will be evaluated by measuring health counselors’ outcomes related to the partner process as well as through hotline calls and web site hits. If data demonstrate an improvement in client participation in PCRS, the program will be promoted statewide.

Influenza Update: Live Attenuated Influenza Vaccine (LAIV) Approved for Healthy Persons Aged 2-49 Years

On September 19, 2007, the Food and Drug Administration (FDA) approved the use of live attenuated influenza vaccine (LAIV - FluMist®), the nasal spray flu vaccine, for healthy children ages 2-4 years (24-59 months old) without a history of recurrent wheezing, as well as for healthy persons ages 5-49 years who are not pregnant.

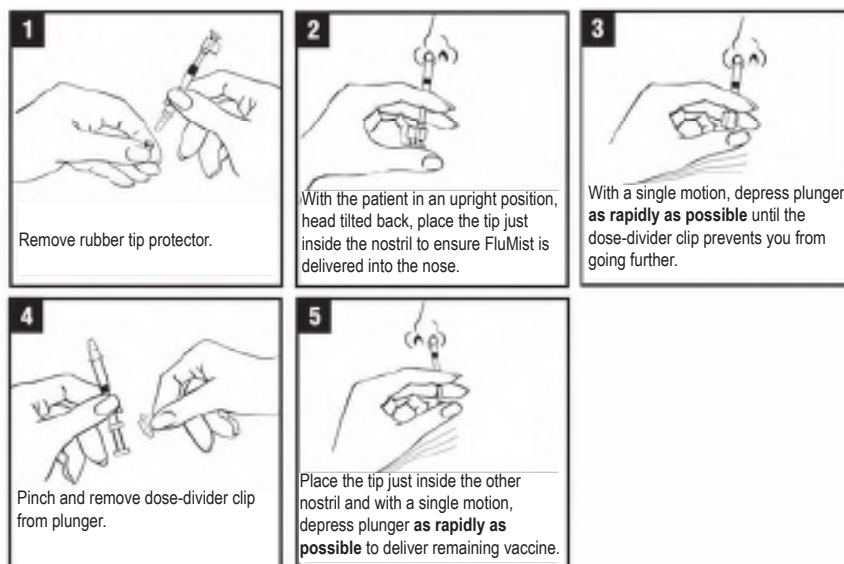
Children ages 2-8 years who are receiving influenza vaccine for the first time, and those vaccinated for the first time during the previous influenza season but who only received one dose in that previous season, should receive two doses, spaced at least one month apart. Note that the minimum amount of time between the first and second doses of LAIV for children 2-8 years who require two doses has

been changed from six weeks to **four weeks**—therefore, the number of days between the first and second doses of vaccine is now the same for LAIV as it is for trivalent inactivated influenza vaccine (TIV). Also of note, the first and second doses of influenza vaccine do not have to match; live or inactivated vaccine can be used for either dose.

For all individuals, including children age 2-8 years who have previously received influenza vaccine, a dose is considered to be 0.2 mL (given as 0.1 mL per nostril).

LAIV is contraindicated in children and adolescents (2-17 years of age) receiving aspirin therapy or aspirin-containing therapy; in addition, do not use LAIV in children <5 years old with a history of recurrent wheezing.

Additional information is available from the FDA at www.fda.gov/CBER/label/flumistLB.pdf, and the Centers for Disease Control and Prevention at www.cdc.gov/flu/about/qa/nasalspray.htm.



Cases of Selected Notifiable Diseases Reported in Virginia*

Total Cases Reported, August 2007									
Disease	State	Regions					Total Cases Reported Statewide, January - August		
		NW	N	SW	C	E	This Year	Last Year	5 Yr Avg
AIDS	79	5	27	4	18	25	434	370	446
Campylobacteriosis	53	15	13	9	10	6	377	397	426
Chickenpox	9	0	1	0	2	6	961	1,204	550
<i>E. coli</i>, Shiga toxin-producing	15	7	5	1	1	1	95	96	47
Giardiasis	40	4	11	13	7	5	298	263	265
Gonorrhea	607	35	52	57	200	263	4,063	4,303	5,638
Group A Strep, Invasive	4	0	0	2	1	1	110	96	73
Hepatitis, Viral									
A	5	1	1	1	2	0	59	37	57
B, acute	4	0	1	2	1	0	92	36	109
C, acute	0	0	0	0	0	0	5	6	8
HIV Infection	116	6	23	13	29	45	559	597	563
Lead in Children†	65	9	4	16	22	14	345	419	442
Legionellosis	5	1	2	2	0	0	26	37	36
Lyme Disease	83	12	60	6	2	3	490	158	102
Measles	0	0	0	0	0	0	0	0	0
Meningococcal Infection	0	0	0	0	0	0	12	15	19
Pertussis	8	0	0	1	1	6	75	133	136
Rabies in Animals	68	14	8	21	12	13	488	405	371
Rocky Mountain Spotted Fever	10	1	1	3	4	1	69	66	33
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	84	9	34	14	17	10	614	592	666
Shigellosis	21	0	5	2	3	11	99	45	227
Syphilis, Early§	47	0	15	3	15	14	252	213	151
Tuberculosis	17	0	8	2	7	0	155	174	174

Localities Reporting Animal Rabies This Month: Accomack 1 raccoons Alexandria 2 raccoons; Alleghany 1 skunk; Amelia 1 fox; Appomattox 1 raccoon; Arlington 4 raccoons; Augusta 1 raccoon, 1 skunk; Bath 1 skunk; Bedford 1 skunk; Botetourt 1 skunk; Buckingham 1 fox; Campbell 1 raccoon; Carroll 1 skunk; Charles City 1 raccoon; Charlotte 1 fox; Craig 1 raccoon; Cumberland 1 raccoon; Fauquier 2 skunks; Frederick 1 groundhog; Galax 2 skunks; Gloucester 2 raccoons; Grayson 1 raccoon; Halifax 1 raccoon; Hanover 1 fox, 2 skunks; Highland 1 raccoon; Lynchburg 1 raccoon; Mecklenburg 1 skunk; Norfolk 1 raccoon; Northampton 1 raccoon; Northumberland 1 fox; Nottoway 1 skunk; Prince George 1 fox; Prince William 1 groundhog, 1 raccoon; Pulaski 1 skunk; Richmond 1 fox; Roanoke 1 bat; Roanoke City 1 bat; Rockingham 1 skunk; Salem 3 bats; Shenandoah 1 raccoon; Southampton 1 skunk; Spotsylvania 1 raccoon, 1 skunk; Stafford 1 raccoon; Suffolk 2 raccoons, 1 skunk; Tazewell 1 bat; Virginia Beach 1 fox; Warren 1 raccoon, 1 skunk; Washington 1 raccoon; Westmoreland 1 fox; Wythe 2 skunks.

Toxic Substance-related Illnesses: Adult Lead Exposure 11; Mercury Exposure 1; Pneumoconiosis 4.

*Data for 2007 are provisional. †Elevated blood lead levels $\geq 10\mu\text{g/dL}$. §Includes primary, secondary, and early latent.

Epi-Fact: VaCARES

The Virginia Congenital Anomalies Reporting and Education System (VaCARES) is the Commonwealth's birth defects registry. Every hospital, as mandated by the *Code of Virginia* § 32.1-69.1, reports to the Virginia Department of Health (VDH) any child under two years of age who is diagnosed with a birth defect. Eighty-six different categories of structural, functional, or biochemical anomalies are required to be reported. Data are sent to VDH via the Virginia Infant Screening and Infant Tracking System (VISITS), an online integrated database. Also, data obtained from Virginia Newborn Screening

Services are entered into the VaCARES database along with data from birth and death certificates filed with the State Registrar of Vital Records and data from the Virginia Early Hearing Detection and Intervention Program. VaCARES is managed by the VDH Division of Child and Adolescent Health, Pediatric Screening, and Genetic Services.

Annual VaCARES data are reported by VDH to the National Birth Defects Prevention Network (NBDPN) for its *Congenital Malformation Surveillance Report in the United States*. Birth defects with the highest incidence in Virginia for 1999-2003 were (1) patent ductus arteriosus (60 per 10,000 live births), (2) atrial septal defect

(43 per 10,000 live births), (3) ventricular septal defect (30 per 10,000 live births), (4) Down syndrome or Trisomy 21 (10 per 10,000 live births), (5) pyloric stenosis (10 per 10,000 live births), (6) pulmonary valve atresia and stenosis (10 per 10,000 live births), (7) obstructive genitourinary defect (9 per 10,000 live births), (8) cleft lip with and without cleft palate (9 per 10,000 live births), (9) congenital hip dislocation (7 per 10,000 live births), and (10) cleft palate without cleft lip (5 per 10,000 live births).

For more information on pediatric screening and genetic services activities in Virginia, go to www.vahealth.org/psgs/