



ISSUE

3

October 31, 2005

A series of CME-certified reports on the human papillomavirus, a leading cause of cervical cancer.

Target Audience:

Developed for primary care physicians, internists, pediatricians, family physicians, and other medical professionals who treat patients at risk for HPV.

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HPV Prevention:

Examining the Potential of New Vaccines and Reappraising Our Messages to Patients



Human papillomavirus (HPV) infection is the most commonly sexually transmitted viral infection in the U.S. today and certain strains can lead to genital warts (condylomata acuminata), dysplastic lesions, and cancer. Although most HPV infections are asymptomatic and benign, HPV causes nearly all cases of cervical cancer, which is the second most common cancer in women throughout the world. The American Cancer Society (ACS) estimates that in 2005, there will be about 10,370 new cases of cervical cancer in the U.S. and 3,710 deaths attributed to it.¹

The number of deaths from cervical cancer has dropped significantly, primarily due to regular cervical cancer screenings and effective treatment. In fact, the U.S. has seen cervical cancer mortality decrease by over 70 percent since the introduction of the Papanicolaou (Pap) test.¹ Despite HPV's significant recurrence rate, there are effective strategies for treating genital warts, dysplastic lesions, and cervical cancer and this, too, is good news.

Of course, the optimal management strategy is to prevent HPV infection and its transmission in the first place. In this issue of Insight HPV, we examine important prevention messages—from abstinence and education to the development of exciting new vaccines.

About this CME Activity:

Please read the publication, reflect on its content, complete the CME Self-Assessment and CME Evaluation, and return them to the address indicated. Upon receipt, your certificate of completion will be sent to you with the correct answers to the CME Self-Assessment. The estimated time a learner will need to complete this self-study activity is .5 hours.

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Learning Objectives

After reading this publication, the participant should be able to:

- 1) Identify the HPV types that cause most cases of genital warts and cervical cancer;
- 2) Discuss with patients the roles of abstinence, "safer" sex, alcohol and drug use, education and vaccines in the prevention of HPV infection;
- 3) Review key clinical data from monovalent, bivalent and quadrivalent vaccine trials; and
- 4) Evaluate the potential impact of an effective vaccination program for HPV.

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Acknowledgement

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The following experts and planners indicated they have no potential conflicts of interest to disclose relative to this activity:

Jeffrey Lin, MD and **Daniel Reichard, GWUMC**
Director of CME

The experts listed below disclosed relationships with outside interests, as indicated. The experts' editorial contributions were independently validated by GWUMC faculty with expertise in HPV vaccines.

J. Thomas Cox, MD: Dr. Cox participates in speakers' bureaus for Digene and 3M Pharmaceuticals. He also serves as a consultant to Digene and 3M Pharmaceuticals. Dr. Cox serves on the data and safety monitoring board for Merck & Co.'s worldwide quadrivalent HPV vaccine.

Martin C. Mahoney, MD, PhD: Dr. Mahoney has served on an advisory board for Merck & Co.

THE HPV PREVENTION MESSAGE: A CALL TO ACTION

J. THOMAS COX, M.D.

Human Papillomavirus (HPV) infection is the most common sexually transmitted viral disease (STD) in America. Anyone who has ever had sexual relations has a chance of being exposed to the HPV virus. As with all STDs, finding effective prevention strategies is a challenge; this is particularly true for HPV infections, which are very common, easily transmitted, and not prevented by condom use.

Certainly, regular cervical cancer screening for all sexually active women and the treatment of precancerous lesions remain key strategies for reducing the risk of cervical cancer, a rare but deadly consequence of HPV infection. (See the discussion of screening guidelines in the Summer 2005 issue, available at TargetHPV.org.) However, screening does *not* prevent HPV infection or the development of precancerous lesions. The introduction of HPV vaccination, discussed elsewhere in this issue, represents an exciting new development for preventing infection with the most common HPV types. However, these HPV vaccines are not yet available; furthermore, when they become available, they will be most effective in those who have not begun sexual activity.

So, what are the other prevention strategies?

Condoms. The results of a recent literature survey suggest that condom use may protect against genital warts, CIN II or III, and invasive cervical cancer.² However, it's important to stress that the use of condoms cannot protect entirely against HPV. Human papillomavirus is spread by skin-to-skin contact and does not require a transfer of body fluids. Since HPV may shed beyond the covered area, condoms do not provide as complete protection as they do for some other pathogens, such as HIV and gonorrhea. Although the Centers for Disease Control (CDC) recommends the use of condoms, patients should understand that condoms do not offer 100 percent protection against an HPV infection.

Abstinence. Avoiding skin-to-skin contact with someone with an HPV infection is the most effective strategy to prevent HPV transmission. Refraining

from genital contact with another individual (i.e., having no sexual activity) is the only sure way to eliminate the risk for future genital HPV infections. Unfortunately, there is no such thing as truly “safe sex.”

Lifelong mutual monogamy. There is no question that the more partners one has, the higher the risk for infection with any STD. Given the strong association between number of sex partners and HPV infection, faithfulness to one partner would likely decrease the probability of acquiring an HPV infection. So for those who choose to be sexually active, a monogamous relationship with an uninfected partner is a good strategy to prevent genital HPV infection. For those who are not in a long-term mutually monogamous relationship, reducing the number of sex partners may also reduce the risk.

Future options. In addition to developing new HPV prophylactic vaccines, researchers are trying to identify specific biomarkers for screening or triage of women with high-risk HPV infections. One marker of oncogen-

ic HPV expression, the p16^{INK4a} protein, has shown some promise in identifying high-grade CIN. Further studies are needed to determine how useful this marker would be in predicting the risk for developing CIN III.

Education. Good communication with our patients about HPV will be key. A wealth of good information is available on STDs—and so is a lot of confusion and denial. With the introduction of the prophylactic vaccines, patients will surely be hearing more about HPV in the near future.



PREVENTING GENITAL HPV INFECTION: STRATEGIES FROM THE CDC

Screening. Regular cervical cancer screening for all sexually active women and treatment of precancerous lesions remain the key strategies for prevention of cervical cancer.

Abstinence. The surest way to eliminate the risk for future genital HPV infections is to refrain from any genital contact with another individual.

Monogamy. For those who choose to be sexually active, a long-term, mutually monogamous relationship with an uninfected partner is the strategy most likely to prevent genital HPV infections. However, it is difficult to determine whether a partner who has been sexually active is currently infected.

Fewer sex partners. For those who choose to be sexually active and are not in long-term, mutually monogamous relationships, reducing the number of sex partners and choosing a partner less likely to be infected may reduce the risk of genital HPV infection. Partners less likely to be infected include those who have had no or few sex partners.

Condoms. While available scientific evidence suggests that the effect of condoms in preventing HPV infection is unknown, condom use has been associated with lower rates of the HPV-associated diseases of genital warts and cervical cancer. However, the available scientific evidence is not sufficient to recommend condoms as a primary prevention strategy for the prevention of genital HPV infection.

Vaccines. In the future, receiving a safe and effective HPV vaccine to help prevent genital HPV infection—as well as genital warts and cervical cancer—would be an important prevention measure. However, an effective HPV vaccine would not totally replace other prevention strategies.

Adapted from: Report to Congress, Prevention of Genital Human Papillomavirus Infection, Centers for Disease Control and Prevention, January 2004. http://www.nccp-online.org/hpv_report_jan%202004.pdf



PREVENTION OF HPV WITH VACCINES: CLINICAL TRIAL RESULTS SHOW PROMISE

MARTIN MAHONEY, M.D.

Several HPV vaccines are currently under investigation. Unlike other prevention approaches described in this newsletter, HPV vaccines reduce susceptibility to infection by stimulating the immune system. Human papillomavirus vaccines aim to prevent HPV-associated sequelae (genital warts, cervical cancer precursors, and cervical cancer) by preventing HPV infection altogether, or by reducing the persistence of any infection that does occur. These new HPV vaccines are showing promising results in clinical trials, which are summarized briefly below.

Monovalent vaccine. In the first trial published by Koutsky et al. in 2002,³ a three-dose regimen of a prophylactic vaccine containing only one type of HPV, the oncogenic HPV-16, proved highly efficacious in reducing the incidence of persistent infection with HPV-16.

This double-blind randomized study was conducted in 2,392 women, ages 16 to 23 years, who were randomly assigned to receive three doses of either placebo or HPV-16 virus-like-particle (VLP) vaccine (40 µg per dose), given at day 0, month 2, and month 6.



OVERVIEW OF HIGH-RISK AND LOW-RISK HPV TYPES

Human papillomavirus is not a single virus but a family of closely related viruses, each designated as a “type” based on nucleic acid sequencing. More than 100 HPV types have now been described, including more than 35 that affect the genital tract. The types that are included in the clinical-trial vaccines reported in this issue include:

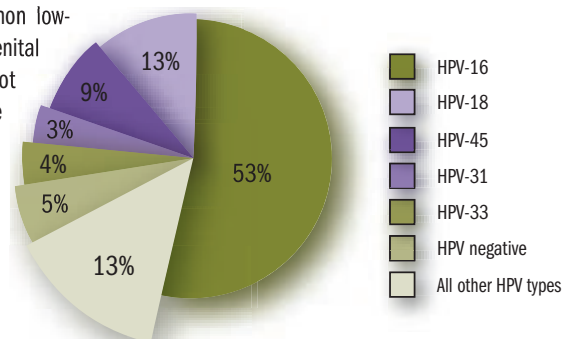
HPV-16 and HPV-18. These types are referred to as “high-risk” because of their association with malignancies. Although a number of high-risk HPV types have been associated with cervical cancer, about 70 percent of cervical cancers are due to HPV-16 and HPV-18. (See **Figure 1.**) HPV-16 is mainly associated with squamous cell cancers; HPV-18 is usually associated with adenocarcinomas, although it can be found in squamous carcinomas as well. HPV-16 is included in all three of the vaccines used in the Phase II clinical trials discussed in this newsletter. HPV-18 is included in the bivalent and quadrivalent vaccines.

HPV-6 and HPV-11. These types are considered “low-risk” because they are rarely, if ever, found in cancers. Disease caused by the low-risk types most commonly present as papillary condylomas (classic genital warts), but may also present as flat lesions that may or may not be visible to the unaided eye. HPV-6 and HPV-11 are the most common low-risk types and account for 90 percent of all genital warts. Although HPV-6 and HPV-11 are not linked to cervical cancer, they can cause abnormal Pap smears, which then lead to additional tests and anxiety about cancer. HPV-6 and HPV-11 are included only in the quadrivalent vaccine.

Figure 1



HPV Types That Cause Cervical Cancer: A Worldwide Survey



Munoz et al 2003 n=1918



The investigators tested for the presence of HPV-16 DNA in genital samples obtained at enrollment, one month after the third vaccination, and every six months thereafter for 36 months. A persistent HPV-16 infection was defined as the detection of HPV-16 DNA in samples obtained at two or more visits. HPV-16-related cervical intraepithelial neoplasia (CIN) occurred in nine cases, all of whom were placebo recipients.

The incidence of persistent HPV-16 infection was 3.8 per 100 woman-years at risk in the placebo group and 0 per 100 woman-years at risk in the vaccine group, indicating 100 percent efficacy for the vaccine ($P < 0.001$). The seroconversion rate was 99.7 percent.

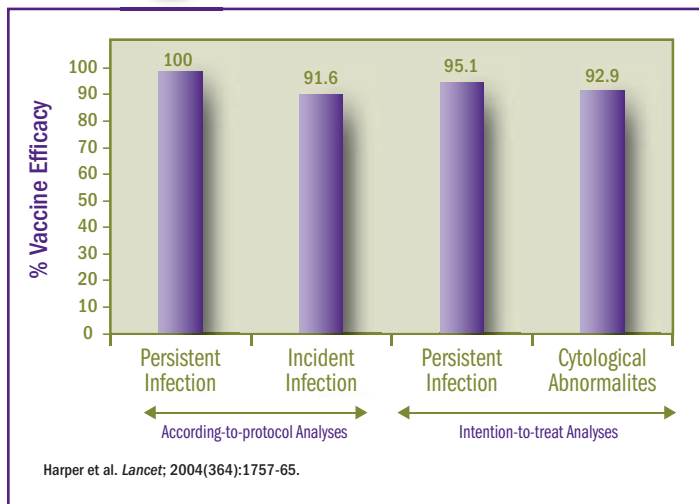
Bivalent vaccine. The results of an international trial of a bivalent prophylactic HPV vaccine were published by Harper et al. in 2004.⁴ This vaccine contains HPV-16 and HPV-18, the two most common oncogenic HPV types.

This randomized, double-blind, controlled trial included 1,113 women, ages 15 to 25 years who received three doses of either the vaccine or placebo on a 0-month,

1-month, and 6-month schedule. Women were followed for up to 27 months and evaluated for HPV infection (by cervical cytology and self-obtained cervicovaginal samples), as well as for vaccine safety and immunogenicity.

The vaccine was 100 percent effective against persistent infection with HPV-16/18, and 91.6 percent effective against incident infection. (See **Figure 2**.) In the intention-to-treat analyses, which included all women who were randomized, vaccine efficacy was 95.1 percent against persistent cervical infection with HPV-16/18 and 92.9 percent against cytological abnormalities associated with HPV-16/18 infection. Antibody responses were induced in 99.8 percent of the subjects. Antibody titers in the vaccine group were 80-fold higher for HPV-18 and 101-fold higher for HPV-16 when compared to those elicited by immune responses to natural viral infections. This vaccine was generally safe, well tolerated, and highly immunogenic.

Figure 2  **HPV 16/18 Bivalent Vaccine Efficacy**



Quadrivalent vaccine. The results of the most recent phase II HPV vaccine trial were published by Villa et al. in 2005.⁵ The vaccine in this study consisted of four HPV types, including the two associated with about 70 percent of cervical cancers (HPV-16 and HPV-18) and two associated with 90 percent of genital warts (HPV-6 and HPV-11).

This randomized, double-blind placebo-controlled study included 552 women, ages 16 to 23 years. Subjects received either vaccine or placebo on day 1, month 2 and month 6, and were followed for 30 months. The

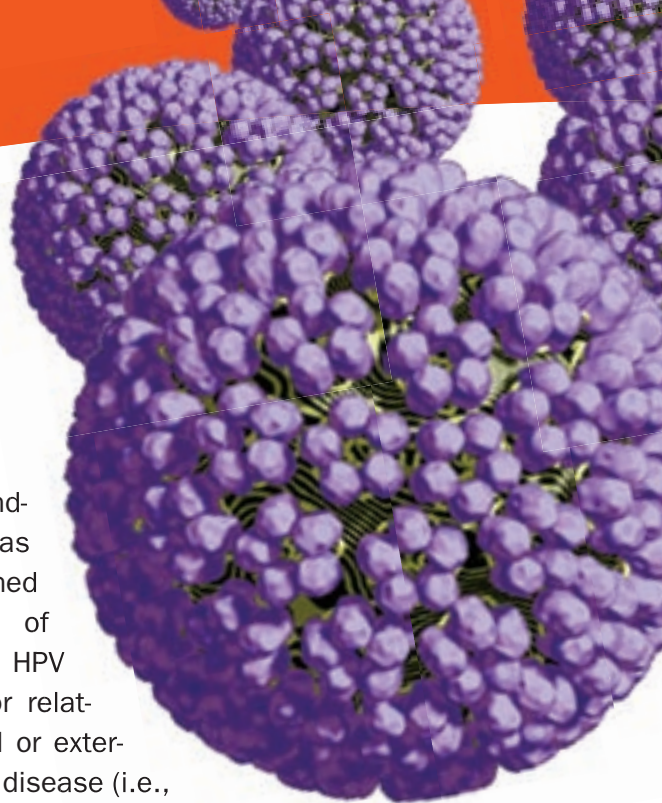
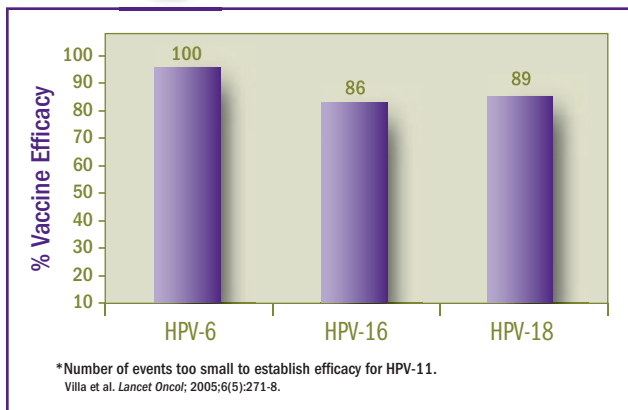


Figure 3



Quadrivalent HPV Vaccine Efficacy by HPV Types



primary endpoint was the combined incidence of persistent HPV infection or related cervical or external genital disease (i.e., CIN, cervical cancer, or external genital lesions) caused by the HPV types in the vaccine. The results showed that the vaccine efficacy was 90 percent for the primary endpoint. For the individual HPV types, vaccine efficacy was 100 percent for preventing HPV-6, 86 percent for HPV-16, and 89 percent for HPV-18. (The number of events was too small to establish efficacy for HPV-11). (See **Figure 3.**) The vaccine was generally safe and well-tolerated with no vaccine-related serious adverse events reported. (See **Table 1.**) There was a slightly higher rate of pain at the injection site in the vaccine group compared to the control group; systemic effects were comparable.

A multicenter Phase III trial of the quadrivalent vaccine is currently underway in several countries. This study will enroll about 11,500 women, ages 19 to 23 years old, and assess efficacy, immunogenicity and safety over five years of follow-up.

Summary

The results from these randomized clinical trials of HPV vaccines are encouraging. The vaccines showed high efficacy in preventing HPV infection and high levels of immunogenicity, and were generally safe and well tolerated. The duration of efficacy remains a key issue that could have an impact on vaccination strategies, however, like other new vaccine products, this issue will need further study. (See **Table 2.**)

Table 1



Adverse Events

	VACCINE	PLACEBO
AEs REPORTED	92%	88%
Injection Site	86%	77%
Systemic	69%	69%
VACCINE ASSOCIATE AEs	89%	82%
Injection Site	88%	77%
Systemic	38%	33%
SERIOUS AEs	1%	1%



Table 2



Preventing HPV Infection: Phase II Trials of Prophylactic HPV Virus-like Particle (VLP) Vaccines

	MONOVALENT	BIVALENT	QUADRIVALENT
HPV TYPES	16 (high-risk)	16, 18 (high-risk)	16, 18 (high-risk) 6, 11 (low-risk)
SUBJECTS	2392 women (ages 16 to 23 years)	1113 women (ages 15 to 25 years)	552 women (ages 16 to 23 years)
DOSING/ SCHEDULE	40 µg (HPV-16) at 0, 2 and 6 months	20 µg (HPV-16) 20 µg (HPV-18) at 0, 1 and 6 months	20 µg (HPV-6) 40 µg (HPV-11) 40 µg (HPV-16) 20 µg (HPV-18) at 0, 2 and 6 months
ENDPOINTS	1° - Persistent HPV infection 2° - Tolerability	1° - Persistent HPV infection 2° - Cytologically detected CIN or cancer	1° - Combined incidence of persistent HPV infection or related genital disease (CIN, cervical cancer, genital warts)
FOLLOW-UP	17.4 months	27 months	30 months
OUTCOMES	100% efficacy preventing persistent HPV-16 infections, and HPV-16-specific CIN.	100% efficacy preventing persistent HPV-16 and HPV-18 infections. 93% efficacy preventing cytological abnormalities.	100% efficacy for combined endpoint for HPV-6; 86% for HPV-16; and 89% for HPV-18. (The number of events was too small to establish efficacy for HPV-11). Overall, 90% efficacy in preventing persistent infection or related genital disease associated with all 4 types.
SERIOUS ADVERSE EFFECTS	<1%; no significant difference by group	~4%; no significant difference by group	1%; no significant difference by group



HPV VACCINE DEVELOPMENT: DISCOVERY OF “VLP L1” VACCINES

A major breakthrough in HPV vaccine research came in the mid-1990s, when researchers found that they could use recombinant technology to develop genetically engineered, immunologically active, virus-like particles (VLPs). They used the viral L1 gene to produce VLPs, and found that these “L1 VLPs” induced

high levels of neutralizing antibodies in both animals and in humans.

The VLPs closely resemble native HPV particles, but are devoid of DNA and are therefore noninfectious. However, the immune system perceives the VLPs as

infectious viruses and responds with strong antibody and cell-mediated immune responses. So far, VLPs have been produced for at least ten HPV types.

The vaccines currently under investigation in the trials discussed here are all VLP L1 HPV vaccines.



HPV VACCINES: CAN THEY MAKE A DIFFERENCE?

MARTIN MAHONEY, M.D.

HPV infection results in a significant disease burden that is both costly (from the health care system perspective) and distressing (from a patient perspective). While screening is a key strategy for lowering the risk of cervical cancer, our best, most promising strategy against HPV infection is prevention. Based on clinical trials completed to date, adding a successful HPV vaccination program to the other prevention strategies discussed in this issue will have a significant impact on the morbidity and mortality associated with HPV infection.

Cervical cancer and abnormal Pap smears. The HPV vaccine is probably the first vaccine that could have a significant impact on cancer morbidity and mortality. If introduced worldwide, HPV vaccination could prevent a large proportion of the nearly 470,000 cases of cervical cancer that occur each year.⁶ Most cervical cancers are due to only a few HPV types—with types 16 and 18 responsible for the majority of the cancers. If women were vaccinated against these types of HPV before they became sexually active, we could expect to see a significant reduction in the risk of cancer.

A vaccine including only types 16 and 18 could theoretically prevent 70 percent of cervical cancers.

Because of the long period of time involved in the progression of an HPV infection to cancer, a reduction in the incidence of cervical cancer would not be apparent for 20 to 25 years. On the other hand, within a short time interval, we could expect to see a dramatic reduction in abnormal Pap smears—in everything from atypical squamous cells of undetermined significance (ASCUS) to low-grade and high-grade dysplasias.

Genital warts. Genital warts are remarkably common, occurring in about one percent of the population. New cases number from 500,000 to 1 million a year.⁷ Although genital warts are not linked to cancer, they can be painful, disfiguring, and psychologically distressful. Treatment can be painful as well, and expensive. Genital warts are very contagious and chronic infections are common. Because HPV-6 and HPV-11 are responsible for 90 percent of all cases of genital warts, a vaccine that included these types could have a significant impact.



HOW WE KNOW THEY WORK: MEASURING HPV VACCINE EFFICACY

In cancer prevention studies, the incidence of cancer itself has traditionally been the measurable endpoint to assess the efficacy of a particular intervention. However, in the case of cervical cancer, we must use a surrogate endpoint—not invasive cancer—because of time and ethical considerations. Trials with an endpoint of invasive cancer would be prohibitively large and lengthy. Furthermore, because cervical cancer can be prevented through proper detection

and treatment, a study endpoint of cancer would not be ethical.

So, how is efficacy measured in HPV vaccine clinical trials? The U.S. Food and Drug Administration Vaccines and Related Biologicals Advisory Committee decided that the primary endpoint for vaccine licensure in the U.S. should be detection of histologically-classified cervical intraepithelial neoplasias (CIN) of moderate

or high-grade (CIN II/III), as well as cancer.⁷ Virological measurements of infection are also useful, since persistent infection with the same high-risk type is considered a predictor for moderate- or high-grade cervical dysplasias and cancer. Theoretically, if a vaccine is effective against transient or persistent HPV infections, it is likely that it will protect against cervical cancer.



Target populations and vaccine administration. To be effective, a prophylactic HPV vaccine should be administered before infection in order to elicit neutralizing antibodies to inhibit attachment or entry of the virus. Because HPV is easily and frequently transmitted via skin-to-skin contact, a vaccination program might be most effective when implemented before the onset of sexual activity. Thus, the target population that is being considered for prophylactic HPV vaccination is children, ages 9 to 12 years, who have not reached the age of sexual maturity, and adolescents and young adults who have not begun sexual activity. In order to achieve peak immune response, the HPV vaccines would require three injections, similar to the vaccination schedule for Hepatitis B.

Although HPV-associated ano-genital cancers do occur in men, they are much rarer than in women, so vaccination against the oncogenic HPV types would have a negligible benefit in males. However, a vaccine against the nononcogenic types (HPV-6 and HPV-11) could be useful in preventing genital warts in both men and women.

Costs. Although it is too early to discuss a cost/benefit ratio, we would expect that an effective HPV vaccination program that both prevented cancer and reduced the frequency of abnormal Pap smears would remove

a substantial burden from the health care system.

A final word. The preventive HPV vaccines under investigation certainly represent a strong weapon in the arsenal against sexually transmitted diseases. However, patients must also understand that the available vaccines include only four of the many HPV types that can affect the genital tract. While these four HPV types account for a majority of HPV related clinical manifestations (e.g., cervical cancers, high grade premalignant lesions and genital warts), they do not protect against infection by all HPV types. An HPV infection with a less frequently occurring virus type—either oncogenic or nononcogenic—is still possible, as is the acquisition of another type of sexually transmitted infection. As mentioned in the summary, the duration of protection afforded by this vaccine is still not known. Also, a preventive HPV vaccination is intended to complement a cervical cancer screening program, not replace it; routine gynecological exams and Pap smears remain just as important and necessary. Likewise, the availability of a vaccine should not diminish the importance of the other HPV prevention strategies—abstinence and “safe sex”—discussed elsewhere in this issue.

V A WORD ABOUT THERAPEUTIC HPV VACCINES

In addition to prophylactic vaccines, a number of therapeutic vaccines are also in development. Unlike the prophylactic vaccines, the therapeutic vaccines are designed to treat preexisting HPV infection by inducing a specific T-cell mediated response leading to regression of existing lesions.

Most therapeutic vaccines target the HPV oncogenic proteins, E6 and/or E7, which are co-expressed in the majority of HPV-containing carcinomas and are critical to the induction and maintenance of cellular transformation. The goal of therapeutic vaccine use is to prevent the development of lesions, slow the

progression of pre-existing lesions, and eliminate existing lesions or malignant neoplasms.

Although the therapeutic vaccines have shown promising results in preclinical trials, the results of clinical trials of safety and efficacy are still pending.

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For More Information About HPV

The following organizations provide a wealth of information on HPV and cervical cancer:

The **American Social Health Association** (ASHA) sponsors the **National HPV and Cervical Cancer Prevention Resource Center**, which has a web site with facts about HPV, an HPV chat room, and information about HPV support groups. www.ashastd.org/hpvccrc

The **American Society for Colposcopy and Cervical Pathology** (ASCCP) is an organization of health care professionals committed to improving health through the study, prevention, diagnosis and management of lower genital tract disorders. Its website contains educational programs and resources. www.asccp.org

The **American Cancer Society** (ACS) has a web site with information about cervical cancer. www.cancer.org

The **National Cancer Institute** (NCI) provides information on cervical cancer. www.cancer.gov/cancertopics/types/cervical

The **Centers for Disease Control and Prevention** (CDC) has facts and statistics about HPV and cervical cancer and a number of resources for clinicians and educators. www.cdc.gov/std/hpv

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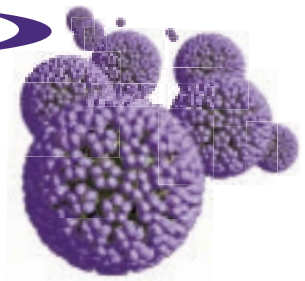
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A series of CME-certified reports on the human papillomavirus, a leading cause of cervical cancer.

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PROGRAM EXAMINATION

- The bivalent vaccine tested in clinical trials contains one "high-risk" and one "low-risk" HPV-type.
 a. True b. False
- A vaccine containing HPV-16 and HPV-18 could prevent approximately what percentage of cervical cancers?
 a. 0% b. 50% c. 70% d. 95% e. 100%
- Which population is expected to be the primary target of an HPV vaccination program?
 a. Young adults with multiple sex partners. b. Women with a history of recurring genital warts. c. Adolescents prior to start of sexual activity.
 d. Women with a history of abnormal pap smears. e. None of the above
- An added benefit of a routine HPV vaccination program is that it will allow women to decrease the frequency of their pap smears.
 a. True b. False
- HPV-6 and HPV-11 are included in the quadrivalent vaccine mainly for protection against:
 a. Genital warts b. Cervical cancer c. All anogenital cancers other than cervical cancer
 d. Abnormal pap smears e. All of the above
- Condoms, when used correctly, are highly effective in preventing the transmission of an HPV infection.
 a. True b. False
- True or False: The vaccines currently under investigation in the trials discussed here are all VLP L1 HPV vaccines.
 a. True b. False
- Which of the following statements about virus-like particles is not true:
 a. VLPs are devoid of DNA b. VLPs are noninfectious c. VLPs induce a strong antibody response
 d. VLPs do not induce a cell-mediated immune response e. VLP vaccines are HPV-type specific
- HPV-6 and HPV-11 primarily cause genital warts and are not associated with abnormal pap smears.
 a. True b. False
- The HPV type included in all three of the HPV prophylactic vaccines evaluated in clinical trials is:
 a. HPV-6 b. HPV-11 c. HPV-16 d. HPV-18 e. None of the above

PROGRAM EVALUATION Please indicate your response to the statements below using the scale indicated.

- This activity better helped me identify the HPV types that cause most cases of genital warts and cervical cancer.
 Strongly Agree Neutral Strongly disagree
 1 2 3 4 5 6 7 8 9 10
- This activity helped me become more aware of the roles of abstinence, "safer" sex, alcohol and drug use, education and vaccines in the prevention of HPV infection.
 Strongly Agree Neutral Strongly disagree
 1 2 3 4 5 6 7 8 9 10
- This activity updated me on key clinical data from monovalent, bivalent and quadrivalent vaccine trials.
 Strongly Agree Neutral Strongly disagree
 1 2 3 4 5 6 7 8 9 10
- This activity helped me evaluate the potential impact of an effective vaccination program for HPV.
 Strongly Agree Neutral Strongly disagree
 1 2 3 4 5 6 7 8 9 10
- This newsletter provided a balanced and objective view of the subject matter.
 Strongly Agree Neutral Strongly disagree
 1 2 3 4 5 6 7 8 9 10
- Based on this experience, you are more likely to participate in future GW activities.
 Strongly Agree Neutral Strongly disagree
 1 2 3 4 5 6 7 8 9 10
- What is your specialty? Family Practice General Practice Internal Medicine Obstetrics/Gynecology Other
 If other, please specify _____
- Please indicate how many years you have been in practice?
 1-5 yrs 6-10 yrs 11-15 yrs 15-20 yrs 21+ yrs
- How would you describe your practice?
 Hospital based Practice based HMO based Other

Please feel free to comment on any aspect of this activity that will be constructive in planning future CME activities.