Even women who are vigilant about their children’s vaccinations tend to neglect their own vaccinations or simply are not aware that the need for certain vaccinations continues throughout adulthood. Vaccinations are an important component of overall health, and healthcare providers should be sure their patients know this. Women, typically their family’s gatekeepers to healthcare, particularly need to understand the importance of staying current with vaccinations.

There are 2 new vaccines to incorporate into women’s routine immunization schedule: the human papillomavirus (HPV) vaccine, indicated for girls and younger women, and the herpes zoster vaccine, indicated for older adults. Educating patients about these new vaccines is crucial to promoting their acceptance and also gives providers the opportunity to offer other needed vaccinations.

HUMAN PAPILLOMAVIRUS AND THE HPV VACCINE

Epidemiology and Impact of HPV

HPV is the most common sexually transmitted infection (STI) in the United States. An estimated 6.2 million Americans become infected with HPV each year, with approximately 20 million currently infected, including about 9.2 million sexually active adolescents and young adults aged 15 to 24 years. This age group accounts for 74% of new HPV infections, and in women younger than 25 years, prevalence of HPV infection ranges from 28% to 46%.

Although sexual intercourse is the typical means of HPV transmission, nonpenetrative sexual contact also may transmit HPV. Infection is initiated when microabrasions in the epithelial layers of the external genitalia or cervix are penetrated by HPV virions, reaching to the basal stem cells where HPV DNA replicates. Vertical transmission from mother to newborn is possible, albeit rare.

For women, risk of HPV infection is highest among those younger than 25 years of age, whose first sexual intercourse is at an early age, and who have multiple sexual partners. In addition, HPV infection is often acquired soon after onset of sexual activity. Nearly 40% of college-age women will acquire HPV infection within 2 years of their first sexual experience. The stage of development of the cervix is another contributing factor in the incidence of HPV infection.

The transformation zone of the cervix is where approximately 99% of cervical cancers occur. The epithelium of this zone is immature at puberty, making very young women particularly vulnerable to STIs, including HPV.

Clinical Manifestations of HPV

HPV infection can manifest as genital warts, low- or high-grade cervical dysplasia, cervical cancer, and recurrent respiratory papillomatosis (RRP), a rare yet potentially fatal condition in children and adults.

Every year in the United States, HPV infection is responsible for an estimated 1 million cases of genital warts; 1.4 million cases of low-grade cervical dysplasia; 330,000 cases of high-grade cervical dysplasia; and 11,150 cases of cervical cancer.

High-risk HPV Types 16 and 18

The median duration of HPV infection is 8 months, with 60% to 75% of HPV-infected women showing HPV negativity after 30 months.

Persistent HPV infection is a serious health concern because it may progress to cervical cancer. Of the 30 to 40 types of HPV that infect the genital areas, HPV types 16 and 18 are responsible for about 70% and 80% of all cases of cervical cancer and cervical adenocarcinoma, respectively, as well as 50% of all high-grade cervical dysplasias and approximately 25% of all low-grade cervical dysplasias (Figure 1).

Low-risk HPV Types 6 and 11

Although low-risk HPV types typically are not associated with cancer, there are significant consequences of infection with these types. Notably, HPV types 6 and 11 are responsible for more than 90% of all cases of genital warts (Figure 1). Currently, 1.4 million Americans...
have genital warts, accounting for more than 300,000 initial visits to physician’s offices annually. Genital warts are most prevalent in young adults, particularly women 20 to 24 years of age (6.2 cases/1000 person years). Although genital warts are almost always harmless physically, they are associated with significant psychological distress. Available treatments for genital warts achieve clearance rates of 60% to 90%. However, these treatments are limited by pain and discomfort and lengthy duration. Also, recurrence rates are relatively high due to persistence of underlying infection. HPV 6 and 11 also cause about 80% of cases of RRP, which is typically spread through vertical transmission of HPV. Treatment for RRP is difficult and usually only palliative, often requiring several surgical procedures to remove the papillomas from the larynx.

Economic Impact of HPV Infection
The annual direct medical cost of HPV-related diseases, which includes treatment of genital warts, precancerous lesions, carcinoma in situ, and invasive cervical cancer, is approximately $5 billion (in 2004 dollars). Treatment costs tend to be proportionate to the grade of initial cytopathic abnormality. Women with negative Pap test results paid an average of $57, whereas women with abnormal Pap test results paid an average of $732 for treatment. Treatment for women with atypical squamous cells was $299, compared with $1,275 for low-grade squamous intraepithelial lesions, $1,509 for atypical glandular cells, and $2,349 for high-grade squamous intraepithelial lesions. These costs do not include treatment of cancer, only resolution of the abnormal Pap test or crossing over to cancer care services.

Indirect costs of treatment for other potential complications resulting from HPV or treatment of HPV-related diseases add further economic and emotional burden. For example, a woman who has undergone treatment for an HPV-related disease may be at greater risk for premature birth or fertility problems.

Role of HPV Vaccine and Its Implications
Screening with the Pap test has reduced the incidence of cervical cancer in the United States by 75%. Despite this dramatic decrease, and more than 50 million Pap tests performed annually, a projected 11,150 new cases of cervical cancer will occur this year, with an estimated 3,670 resulting deaths. With no treatments available for HPV infection, prevention is the most promising way to reduce HPV-related disease morbidity and mortality. A quadrivalent HPV vaccine is now available for the prevention of cervical cancer, cervical/vaginal/vulvar precancers, cervical intraepithelial neoplasia (CIN 1-3), cervical adenocarcinoma in situ (AIS), and genital warts caused by HPV types 6, 11, 16, and 18 in girls and women, specifically ages 9 to 26. By targeting these 4 HPV types and this age range, the vaccine is expected to substantially reduce the burden of HPV-related disease. Approval of the quadrivalent HPV vaccine in June 2006 was based
primarily on 2 phase III studies in young women aged 16 to 26, and
2 vaccination-bridging studies in sexually naïve adolescents aged 9 to
15. In the phase III studies, referred to as Females United To Unilaterally
Reduce Endo-ectocervical (FUTURE I and II) disease, the vaccine
demonstrated 100% efficacy in preventing cervical cancer, all grades of
CIN, AIS, vulvar/vaginal neoplasia or cancer, and genital warts related
to HPV 6, 11, 16, and 18 for up to 2 years in women aged 16 to 23.40,41
Both trials also showed 97% efficacy in women who were not com-
pletely adherent to the vaccination schedule (administered on day 1,
month 2, and month 6). This suggests that even in a “real world” pop-
ulation, the vaccine has the potential to significantly reduce HPV infec-
tion and related diseases (Figure 2).40,41

Ideally, HPV vaccine should be administered to children and adoles-
cents before the onset of sexual activity in order to achieve maximum
protective effect. Studies in boys and girls ages 9 to 15 years support
early vaccination in this age group.42 At 1 month after the third and final
vaccine injection, geometric mean titers of type-specific antibodies
were 1.7 to 2.7 times higher in younger adolescents than those in older
adolescents and young adults aged 16 to 23 also receiving the vaccine.42

It is important to note that HPV vaccination is not a replacement for
routine cervical cancer screening, but should be used in conjunction
with screening. Also, the HPV vaccine is preventive for HPV 6, 11, 16,
and 18 only; protection against diseases caused by other HPV types has
not been demonstrated. HPV vaccine is not indicated for treatment of
existing HPV infection. Side effects occurring in clinical trials of HPV
vaccine were minor and similar in the treatment and placebo groups,
and included injection-site pain, swelling, erythema, and pruritus; and
fever, nausea, and dizziness.40,41,43,44

The known duration of efficacy of HPV vaccine is 5 years. Because
FUTURE II study participants from the Nordic region are at least
3 years ahead of their US counterparts, findings in this cohort will pro-
vide further data on longevity and the need and optimal timing for
booster vaccinations. Recent results from a substudy of this group sug-
gest that the vaccine will provide long-lasting immunity.19

By reducing the incidence of HPV infection, vaccination can be
expected to reduce the incidence of HPV-related diseases, which
would, in turn, reduce the frequency of follow-up screenings, colpos-
copies, and other treatments.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Lidocaine 5% patch1</td>
<td>Short-term benefit; erythema</td>
</tr>
<tr>
<td>Capsaicin1</td>
<td>25% to 35% reduction in pain; burning sensation upon application</td>
</tr>
<tr>
<td>Anticonvulsants1,2</td>
<td>43.2% of patients report pain relief; somnolence, dizziness, memory disturbances</td>
</tr>
<tr>
<td>Tricyclic antidepressants1,2</td>
<td>47% to 67% of patients report pain relief; anticholinergic AEs, sedation, cardiac conduction abnormalities</td>
</tr>
<tr>
<td>Opioid analgesics1,2</td>
<td>38% reduction in pain; CNS- and GI-related AEs, dependence</td>
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Make HPV Vaccine Routine: Gain Patient Acceptance

Most cases of cervical cancer can be prevented by the HPV vaccine. To
fulfill this promise, the vaccine needs to be incorporated into the stan-
dard immunization schedule for appropriate patients. However, to fos-
ter patient acceptance of HPV vaccine, clinicians will need to address a
number of educational, cultural, and family/parental issues.

Health-care providers are the primary source of information for
patients and parents of adolescents about HPV vaccination;7 and patient
education increases acceptance of vaccination.6 Adult patients <26 years
of age need to be educated about the role of HPV vaccination in pre-
venting cervical cancer and other HPV-related complications.

For parents of children at or approaching the target ages for vacci-
cination (29 years), a similar educational approach may be used,
with additional counseling for adults who worry that vaccination
against an STI represents tacit consent to early or promiscuous sexual
activity.6 Parents can be told that the immune response to HPV
antibodies is strongest in adolescents, thereby providing the greatest
protection against HPV-related diseases. This information moves the
focus from sexual activity to optimizing disease prevention.

Adults and adolescents often do not see their health-care providers
regularly or change practitioners frequently; it is therefore important not
to miss a vaccination opportunity.6,23 Often, clinicians who focus on
women’s health also provide general medical care. These clinicians
should be diligent in vaccinating their patients, as well as counseling
patients with daughters at or approaching adolescence, to increase the
likelihood of vaccinating girls at the optimal age (11-12 years, accord-
ing to current recommendations).

VARICELLA-ZOSTER VIRUS AND THE HERPES ZOSTER VACCINE

Epidemiology and Impact of Varicella-Zoster Virus

Varicella-zoster virus (VZV) is responsible for herpes zoster, com-
monly known as shingles. In the United States, more than 90% of
adults have been infected with VZV and are at risk for zoster.51 Of
the 1 million cases of herpes zoster that occur annually, 40% to 50%
are in people 60 years of age and older.52 Severity of herpes zoster,
and the frequency and severity of its complications, also increase with
age.53 Risk factors for herpes zoster include history of varicella
This decline in VZV-CMI, most often related to are other triggers of VZV-CMI decline. permits the re-emergence of VZV infection, which however, it may last for several months or even Neuropathic pain is common in and hyperalgesia, an extreme response to normally painful stim-

Not every Randomized, controlled trials of these therapies have PHN is

51,54

None of 50 – 64 Years of Age

The effect on quality of life can be debilitating, particularly for

Vaccines for a Lifetime

≥

12

advancing age.

typically defined as pain that per sists for more than 3 months after

tors for PHN, and its incidence, severity, and duration increase with

severity of acute herpes zoster and age are the main risk factors for PHN, and its incidence, severity, and duration increase with advancing age.58,59

Patients with PHN often experience allodynia, a condition in which pain is caused by ordinary stimuli, such as clothing rubbing on the skin,60 and hyperalgesia, an extreme response to normally painful stim-

The dermatomal rash characteristic of herpes zoster may be pre-

ceded 1 to 5 days by the prodrome, which involves sensory abnor-

malities that may be constant or intermittent, localized or diffuse, and range from itching to tingling to severe pain.51,54 Not every patient develops the prodrome.55,56 Neuropathic pain is common in the acute phase, and may occur all day, every day. It has been described as sharp, throbbing, burning, stabbing, itching, or hot.64 Neurologic, cutaneous, ophthalmic, or visceral complications may occur during or after the acute phase.

Postherpetic Neuralgia

After the herpes zoster rash heals, usually in 2 to 4 weeks following onset, some patients experience persistent, chronic pain known as postherpetic neuralgia (PHN). It is the most common complication of herpes zoster, affecting 10% to 20% of all patients.57 PHN is typically defined as pain that persists for more than 3 months after rash resolution,56 however, it may last for several months or even years. Severity of acute herpes zoster and age are the main risk factors for PHN, and its incidence, severity, and duration increase with advancing age.58,59

Management strategies for herpes zoster and PHN

Acute herpes zoster is typically treated with antiviral therapy. The antiviral agents acyclovir, famciclovir, and valacyclovir reduce the duration and severity of acute herpes zoster, but should be administered within 72 hours of rash onset for maximum effectiveness.51 Some patients do not experience the prodrome and may not have a completely developed rash by 72 hours, and do not seek medical treatment. The benefits of antiviral therapy administered after 72 hours are not known.

Corticosteroids used in conjunction with antiviral therapy have shown benefit in relieving acute pain and speeding rash healing. However, the adverse effects of corticosteroids limit this therapy to relatively healthy individuals; it should not be used by those with diabetes, hypertension, osteoporosis, glycosuria, or peptic ulcer disease.62 None of the treatments for herpes zoster prevent the development of PHN.62-64

Treatments for PHN include anticonvulsants, tricyclic antidepressants, transdermal lidocaine (lidocaine patch 5%), opioid analgesics, and topical capsaicin.65 Randomized, controlled trials of these therapies have

<table>
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<tr>
<th>TABLE 2. Vaccines for a Lifetime</th>
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<tbody>
<tr>
<td><strong>19 – 49 Years of Age</strong></td>
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<tr>
<td><strong>For all women who do not show immunity</strong></td>
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<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap): initial 3-dose series, then a 1-dose booster every 10 years</td>
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<tr>
<td>Human papillomavirus (HPV): a 3-dose series; for women ≤ 26 years of age</td>
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<tr>
<td>Measles, mumps, rubella (MMR):</td>
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<tr>
<td>Varicella (chickenpox): 2 doses</td>
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<tr>
<td><strong>For women with conditions that put them at risk for the disease</strong></td>
</tr>
<tr>
<td>Influenza: 1 dose every year</td>
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<tr>
<td>Pneumococcal (polysaccharide): 1 or 2 doses</td>
</tr>
<tr>
<td>Hepatitis A: 2 doses</td>
</tr>
<tr>
<td>Hepatitis B: 3 doses</td>
</tr>
<tr>
<td>Meningococcal: 1 or more doses</td>
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demonstrated modest pain relief accompanied by adverse effects that are especially problematic in older patients (Table 1).57,68

Vaccination to prevent herpes zoster and PHN offers enormous potential in reducing the burden of herpes zoster and related complications.

**Role of Herpes Zoster Vaccine and Its Implications**

The herpes zoster vaccine, approved in May 2006, is indicated for use in individuals 60 years of age and older. The vaccine is not indicated for the treatment of herpes zoster or PHN, but it can prevent PHN by preventing herpes zoster.

The herpes zoster vaccine is a more potent formulation of the live, attenuated VZV vaccine that has been used in the United States since 1995 for the prevention of varicella.69 The VZV vaccine has reduced the number of varicella cases by approximately 85%.70 The increased potency of the herpes zoster vaccine boosts levels of VZV-CMI to provide protection in older adults with preexisting immunity through infection with wild-type VZV or latent infection established by the vaccine virus. Initial trials in adults aged 55 to >87 years have shown the vaccine to be safe and well tolerated,68,69 significantly boosting VZV-CMI levels and sustaining them for more than 6 years.70

Approval of the herpes zoster vaccine was based on results from the Shingles Prevention Study, a randomized, placebo-controlled, double-blind phase III clinical trial to evaluate the efficacy of the vaccine in decreasing the incidence and severity of herpes zoster and PHN.63 Participants included 38,546 individuals 60 years of age or older who received a single dose of vaccine or placebo and were followed for an average of 3.1 years (range, 31 days to 4.9 years).

The vaccine reduced the impact of herpes zoster by 61%, as measured by burden of illness, a compilation of incidence, severity, and duration of herpes zoster. In vaccinated individuals who developed herpes zoster, the severity of illness was reduced. The vaccine also significantly reduced the incidence of herpes zoster by 51.3%. In the general population, this translates to the prevention of more than 250,000 cases of herpes zoster every year, based on an estimated incidence of 1 million cases per year. Additionally, the incidence of PHN was reduced by 66.5% in all vaccinated subjects. Throughout the study, the cumulative incidence of herpes zoster and PHN was significantly lower in vaccinated subjects than in those receiving placebo.63

The rate of adverse events was low and comparable between vaccine and placebo recipients, with injection-site rash the most common complaint. However, a substudy found that more vaccine recipients (48%) had injection-site complaints than placebo recipients (17%).63

The herpes zoster vaccine provided 4 years of protection from zoster in the Shingles Prevention Study.63 Further research is necessary to determine the duration of the vaccine and whether a booster will be needed.

**Make Herpes Zoster Vaccine Routine**

The herpes zoster vaccine gives health care providers an opportunity to reduce the incidence of herpes zoster, thereby reducing the significant morbidity associated with the illness as well as the incidence of PHN, and greatly improving quality of life in older adults. An understanding of herpes zoster and its complications can promote vaccine acceptance.

**OTHER RECOMMENDED VACCINES FOR WOMEN**

Healthcare providers are responsible for helping women stay up-to-date with their vaccinations. In addition to the HPV and herpes zoster vaccines (as age appropriate), women should receive vaccines according to the most recent Recommended Adult Immunization Schedule issued by the Advisory Committee on Immunization Practices (ACIP).71 (Table 2). For detailed information, refer to the complete ACIP statement and schedule, available at the Centers for Disease Control and Prevention website: http://www.cdc.gov/nip/publications/acip-list.htm.

**Summary**

Ensuring that patients are aware of the vaccinations recommended for their age and health status, and understand the health benefits that vaccinations provide, is paramount to getting them vaccinated. Healthcare providers are the primary influence in promoting the new HPV and herpes zoster vaccines. Patients place enormous importance on their provider’s recommendations. This is especially important to remember when counseling the parents of young girls about the HPV vaccine. Providing patients with the information and advice they need about these and all vaccines will promote patient acceptance, thereby helping to prevent disease and improve patient care.

**REFERENCES**
