Scientific advancements in the 21st century continue to provide new options for primary care providers to promote health through prevention. Immunization remains a key strategy for prevention and is a benchmark for quality of care. The zoster vaccine has proven to be effective at reducing the incidence and severity of herpes zoster (HZ) and the scourge of postherpetic neuralgia (PHN). Older adults are particularly vulnerable to missing this important intervention, but primary care providers are positioned to champion its use.
Varicella, or chickenpox, long thought of as a benign, often pruritic rash that lasts about a week, is better characterized as a viremia caused by the varicella-zoster virus (VZV) that results in seeding of multiple sensory ganglia. HZ, known commonly as shingles, is a painful rash with distribution along a dermatome which occurs as a result of reactivation of latent VZV in the cranial nerve or dorsal root ganglia.

It has been estimated that 50% of unvaccinated individuals who live to 85 years will develop or will have had HZ. Because T-cell immunity decreases with age, age is the major risk factor for developing HZ. Some experts have theorized that older adults may be at an even greater risk because of the success of pediatric varicella immunization programs. Older adults now experience less natural exposure to VZV during their lifetime because their grandchildren are contracting chickenpox less often due to vaccination programs. Natural exposure to the virus is believed to bolster older adults’ dwindling immunity.

Immunologists have confirmed that HZ is a reactivation of an individual’s childhood virus; nevertheless, the overall effect of childhood immunization for chickenpox on the adult incidence of HZ remains to be seen.

Prompt initiation of antiviral therapy with acyclovir, famciclovir, or valacyclovir has been approved by the US Food and Drug Administration (FDA) and demonstrates a decrease in the severity of acute pain, halting of the propagation of the rash as well as hastening its resolution. To further complicate matters in older adults (and in any individual with chronic kidney disease), prescribers of these antiviral medications should make adjustments to the dose and/or its scheduling based on renal function.

HZ has been associated with simultaneous or subsequent development of Bell palsy, Ramsay Hunt syndrome, transverse myelitis, and even stroke and necessitates ophthalmologic evaluation when it occurs in the trigeminal nerve V1 distribution (Figure 1). In addition to potential severe neurologic complications, the development of HZ is particularly concerning in older adults because anorexia and pain are often debilitating and result in impairment of function, thereby threatening an individual’s independence. Older adults who are treated appropriately with opioids or gabapentin are at increased risk for the development of delirium and falls, which further threatens independence.

PHN is a particularly devastating potential consequence of HZ, in which pain persists beyond 90 days (and even years) after the HZ rash has resolved. The incidence and severity of PHN increase with age. The zoster vaccine was approved by the FDA on the basis of results from a randomized, double-blind placebo-controlled trial. In this study, 6.8% of individuals aged 60 to 69 years in the placebo group with confirmed HZ went on to develop PHN, whereas 18.5% of individuals aged 70 years and older in the placebo group with confirmed HZ went on to develop PHN.

PHN further threatens the independence of older patients in many ways. It has been associated with severe pain requiring prescription medications, which may further promote the cycle of depression, weight loss, and fatigue. A meta-analysis published in 2009 failed to show a significant reduction in the incidence of PHN through the use of antivirals and serves to reinforce prevention as the key strategy.

Physicians and the public are now equipped with an effective approach—a vaccine—to prevent herpes zoster.
Contraindications

The zoster vaccine contains a live, attenuated vaccine and should be avoided in individuals with primary or secondary causes of immunodeficiency; this includes individuals with a hematologic cancer (ie, leukemia, lymphoma), and HIV when CD4 cell count is <200. The immunosenescence associated with normal aging is not considered an immunodeficiency, and therefore advanced age should not be a barrier to vaccination.

High-dose immunosuppressive therapy remains a contraindication for zoster vaccine administration. Any individual who is actively undergoing chemotherapy or radiation for any condition should not receive this vaccination. Experts have recommended delaying vaccination in such instances until at least 3 months following the last administration of these therapies.

Immunization against HZ also should be avoided in patients receiving (a) >20mg/d of prednisone, (b) >0.4mg/kg/wk of methotrexate, (c) azathioprine >3mg/kg/d, or (d) anti-tumor necrosis factor therapy. The American College of Rheumatology has recommended administering zoster vaccination prior to initiating DMARDs (disease-modifying antirheumatic drugs).

Older individuals with multiple chronic medical conditions, and particularly those with multiple prescribers, are at particularly high risk for adverse drug events. Prior to zoster vaccine administration, it is worthwhile to take a focused history regarding medication use, especially those prescribed or administered intravenously or injected by subspecialists (ie, infliximab [Remicade]). For example, an older individual may continue to follow up with routine care from her gynecologist who prescribes and administers denosumab (Prolia) for osteoporosis. Denosumab is a monoclonal antibody that is FDA approved for the treatment of osteoporosis and that has been major efficacy trial published within the same year demonstrated that the vaccine reduced not only the incidence by 51.3%, but also the severity of HZ-associated pain by more than 60%. This trial further established a reduction in the incidence of PHN by 66%. Although vaccination efficacy is reduced in adults aged 70 years and older (compared to that in individuals 60-69 years old) as primary prevention, data demonstrate that PHN prevention is unchanged with age. Experts have indicated that because of both the severity and duration of illness caused by PHN, the routine vaccination of older adults is justified.

The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention has recommended that the zoster vaccine be administered once to individuals aged older than 60 years. In March 2011, the vaccine was FDA approved for use in individuals aged 50 years and older; the ACIP declined, however, to recommend routine immunization in individuals aged 50 to 59 years and recently confirmed its position regarding administration of the vaccine in those aged 60 years and older.

Figure 1. Selected complications of herpes zoster in nonimmuno-compromised persons.

Figure 2. Considerations when administering live attenuated herpes zoster vaccine.
incidence of HZ has been consistently increasing in both men and women, with age.\textsuperscript{18,19} The increased incidence of HZ is likely not fully explained by the varicella immunization pediatric program as discussed earlier. People are living longer and at times are carrying a significant burden of chronic medical conditions, which also increases the probability that the latent VZV will resurface. For example, it was noted in previous studies that treatment for rheumatoid arthritis with TNF inhibitors, steroids, or disease-modifying antirheumatic medications is associated with an increased incidence of HZ.\textsuperscript{20,21}

Despite strong recommendations from an authority such as the ACIP, as well as evidence to support the effectiveness of the vaccine, the incidence of HZ has been consistently increasing in both men and women, with age.\textsuperscript{18,19} The increased incidence of HZ is likely not fully explained by the varicella immunization pediatric program as discussed earlier. People are living longer and at times are carrying a significant burden of chronic medical conditions, which also increases the probability that the latent VZV will resurface. For example, it was noted in previous studies that treatment for rheumatoid arthritis with TNF inhibitors, steroids, or disease-modifying antirheumatic medications is associated with an increased incidence of HZ.\textsuperscript{20,21}

**Timing of the vaccination**

The zoster vaccine can be administered simultaneously with other vaccines, including the pneumococcal vaccine and the influenza vaccine.\textsuperscript{13-15} The new Medicare Annual Wellness Visit offers the primary care provider an opportunity to update vaccination history and to educate older patients about the advantages of this vaccine. Any concerns about side effects or contraindications also could be addressed during the visit.

Although it is well established that there is no role for the zoster vaccine during acute HZ illness, the timing of vaccination following resolution is unclear. Recurrence following a recent episode is relatively rare and it has been demonstrated that cellular immunity following HZ is similar to that generated by the vaccination.\textsuperscript{16,17} Although there is no known harm to do so earlier, some experts believe it is sensible to delay immunization for approximately 3 years following an HZ episode.\textsuperscript{7}

**Provider, practice, and patient barriers**

Despite the evidence supporting the routine use of the zoster vaccine, its use has been poor—less than 16% of
The benefits of herpes zoster immunization persist for at least 5 years—and perhaps longer.

The cost of the zoster vaccine itself also is a major perceived barrier.\textsuperscript{6} When the zoster vaccine was introduced, many of the major insurance carriers did not immediately initiate coverage and reimbursement. Today Medicare and most insurance plans reimburse the cost of the zoster vaccine for eligible individuals. Of course, a patient who is within the “donut hole” of Medicare and those not yet meeting their insurance deductible coverage may incur full financial responsibility for the vaccine’s cost. For uninsured and underinsured patients who do not have vaccine coverage, expense of the vaccine could certainly be a barrier to immunization.\textsuperscript{5}

Overcoming barriers

Although the financial concerns remain a barrier to routine administration, several studies have suggested that routine immunization with the zoster vaccine would result in substantial cost savings.\textsuperscript{29-31}

Inter-professional and inter-disciplinary partnerships are helping to develop strategies to improve patient care and outcomes, and it would be advantageous for physicians to partner with local pharmacies and to assist in vaccination. Pharmacists have access to prescription records for individuals with multiple subspecialists and prescribers and thereby will be better able to avoid administration of the vaccine to persons who are not candidates because of concurrent immunosuppressive therapies. Because pharmacists often have better storage capability, one strategy employed by primary care providers is to have the patient fill the prescription at the pharmacy on the day of the appointment and then present to the office/clinic for vaccination administration. Also, similar to the influenza and pneumococcal vaccines, the zoster vaccine can be administered by pharmacists who obtain permission to administer the vaccine in the pharmacy itself. A novel approach utilized by some includes having those pharmacists themselves collaborate with the health care team to participate in mass vaccination clinics at senior housing or assisted living settings.

The vaccine must be stored in a freezer at temperatures between \(-58^\circ\text{F}\) and \(+5^\circ\text{F}\) until it is prepared and administered to a patient.\textsuperscript{27} Proper storage is essential for both the safety and the efficacy of the zoster vaccine, but may present additional financial barriers within a practice setting—cost of a necessary additional freezer and lack of adequate spacing for the equipment. The diluent necessary to mix in the vaccine would be stored in a separate refrigerator. Recommendations from the National Institute of Standards and Technology further advise that all providers use stand-alone freezers and not combination freezers to store all their frozen vaccines.\textsuperscript{28}

The lack of knowledge of HZ immunization guidelines, schedules, contraindications, and vaccine side effects is a major barrier for providers and patients.\textsuperscript{23,24} In 1 study, only 13.7\% of patients had any communication with their medical providers regarding the zoster vaccine, with 70\% of the patients never having heard about the vaccine before.\textsuperscript{25}

Providers who care for populations of HIV-infected patients scored poorly on a knowledge-based assessment regarding potency of the zoster vaccine (47.5\% correctly answered) and mechanism of reactivation of VZV (66\% correctly answered), noting lack of guidance from the CDC on use of this vaccine in HIV patients.\textsuperscript{26}

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facilities. Clearly such a strategy is most helpful for individuals with functional impairments who likely have limitations with using public transportation and/or driving their own vehicles.

Final notes
There exists an increased risk for HZ and PHN among the aged; therefore older adults should be the primary care provider’s clear target of HZ immunization practices. Primary care providers are in the position to bridge chronic disease management with health promotion through prevention. Diligence in keeping well-informed of advancing medical knowledge, persistence with patient education, and participation in novel approaches to promote HZ immunization will help primary care physicians overcome barriers and yield fruitful patient-oriented outcomes.

References

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