Just Say No to Shingles! The Zoster Vaccine

Update for the Clinical Nurse Specialist

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I am a community health CNS. Over the past two years, we have seen a steady rise in shingles in our patient population. Drugstores are offering the “shingle shot” and advertising heavily in our area. Patients are reluctant to obtain the zoster vaccine related to cost and fears regarding any vaccine. How effective is the shingle shot? What is available for patient education?

Nearly 1 million new cases of shingles occur each year in the United States. The current life time risk for shingles is 25% and believed to be related to age-related decline in cell-mediated immunity. Risk for shingles is expected to rise as the baby boomer generation age and numbers of chronically immunocompromised persons related to chemotherapy or organ transplantation increase. Shingles has significant symptom burden and risks for postherpetic neuralgia (PHN), vision loss, scarring, and bacterial superinfection. Although antivirals are effective, treatment must be initiated within 72 hours of symptoms to achieve maximum benefit.

Analysis of geographical mutations in the varicella-zoster virus (VZV), which causes chicken pox (varicella) and shingles (zoster), and the human genome suggests that VZV has traveled with human beings for hundreds of thousands of years. The shingles vaccine offers significant opportunity to decrease the symptom burden of shingles. The herpes zoster (HZ) or shingles vaccine boosts varicella-zoster virus–specific cell-mediated immunity in older persons.

In a clinical trial of 40,000 adults aged 60 years or more, the HZ vaccine reduced the incidence of shingles by 51% and PHN by 67%. Furthermore, persons who developed shingles after receiving the vaccine had significantly shorter median duration of pain and discomfort, lower severity of illness scores, and less interference in activities of daily living. In a continuation trial with more than 14,000 patients, the HZ vaccine effectiveness extended more than 7 years in reducing the incidence of HZ, PHN, and symptom intensity.

PATHOPHYSIOLOGY
Shingles or zoster is a localized, painful cutaneous eruption caused by reactivation of latent VZV decades after initial infection in older adults and immunocompromised persons. Affecting only human beings, VZV infection usually occurs during childhood (varicella) where the virus gains access to epidermal cells and enters sensory nerves. Cell-mediated immunity prevents reactivation within the neuron and inhibits full clinical expression of VZV as zoster. Although virtually all adults have VZV, predicting who will develop zoster remains inexact.

Virions make a home in neuronal cell bodies in sensory dorsal root ganglia near the spinal cord. Although noninfectious in dormant form, when activated later in life or during an immunocompromised state, VZV forms intact virions. Viral particles in the trigeminal or dorsal root ganglion travel along the axons to sensory terminals in the face or chest. A rash manifests when the virus escapes from the nerve terminals and moves into the skin, which triggers an inflammatory response. This inflammation is believed to be responsible for sensitizing nociceptors, which increases the intensity of pain. In some persons, pain may be prodromal or may occur before a rash appears or without a visible rash at all (zoster sine herpete). Healing of the cutaneous rash is thought to coincide with the cessation of viral replication. However, when viral replication ceases in the peripheral ganglia and CNS is unknown.

Postherpetic neuralgia is a chronic and often disabling outcome of zoster that can last for months or years. For
Although neuronal injury happens originally, which became available in the United States in 1995. (See package insert for specific prescribing information. Available at: http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM132831.pdf. Accessed September 20, 2011.) Persons who report a previous zoster event or with a chronic condition such as chronic renal failure, diabetes mellitus, pulmonary disease, or rheumatoid arthritis can receive the vaccine unless the person has conditions that are contraindicated.4 (See package insert for specific prescribing information. Available at: http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM132831.pdf. Accessed September 20, 2011).

The shingles vaccine is never to be used to treat acute zoster or used to prevent the development of PHN in persons with acute zoster. In addition, the vaccine cannot be used to treat chronic PHN. Serologic testing for varicella immunity is not necessary. Zoster is not licensed for persons younger than 60 years and is not recommended for persons of any age who have received the varicella vaccine,4 which became available in the United States in 1995.

Zoster vaccine can be administered with other vaccines such as Td, Tdap, and influenza vaccines without negative affects on humoral immune response. Each vaccine must be administered using separate syringes using different anatomic sites. If simultaneous administration is not possible, zoster vaccine can be given any time before or after an inactivated vaccine and at least 4 weeks before or after a live attenuated vaccine.4 Be mindful that recent evidence suggests that Zostavax and Pneumovax 23 may be more effective given separately over a 4-week interval. In a double-blind placebo-controlled clinical trial of 473 adults, evidence suggested that concomitant administration resulted in decreased Zostavax efficacy.8

Acyclovir (zovirax), famciclovir (famvir), and valacyclovir (valtrex) are effective against the herpes virus family and may attenuate vaccine effectiveness. Persons using antivirals chronically should discontinue use for at least 24 hours before receiving the zoster vaccine and, if possible, abstain from use for 14 days until immunological benefits are established.4

Vaccination does not require assessment of history of varicella (chickenpox) or serologic testing to assess varicella immunity. Zoster vaccine should not be given to persons with a history of anaphylaxis to vaccine components including gelatin and neomycin. Persons with primary or acquired immunodeficiency such as leukemia, lymphomas, or malignant neoplasm of the bone marrow or lymphatic system also should not receive the vaccine. Persons in remission who have not received chemotherapy or radiation for 3 months can receive the vaccine. Other conditions where the vaccine should not be given include AIDS or other clinical manifestations of HIV infection. Check specific recommendations on the Centers for Disease Control and Prevention Web site, as well as the drug labeling for further information. Careful assessment on a case-by-case basis can help determine the risks and benefits of therapy. Vaccination should be

those with zoster, the risk of developing PHN is 10% to 18%. In 10% to 25% of zoster events, the eye involvement can occur, which is associated with pain, scarring, and potential loss of vision.4 Although neuronal injury happens for every patient with shingles, injury does not completely explain the development of PHN pain. Evidence supporting ongoing viral replication in the central nervous system to explain chronic PHN remains weak.2

Patients report pain as mild to severe, occurring for just a few minutes or continuously. Postherpetic neuralgia pain severely impacts quality of life, particularly work, sleep, relationships, and mood. Additional complications may include conjunctivitis, optic neuritis, glaucoma, Bell’s palsy, pneumonia, hepatitis, encephalitis, and even disseminated intravascular coagulopathy from organs seeded with VZV viremia.4

Other persons at risk for zoster are children and adults with hematologic malignancies and solid tumors. Zoster commonly occurs after hematopoietic stem cell transplantation and after organ transplantation. Risk for zoster is very significant for persons with HIV infection. Other risk factors include female gender, white race, and trauma.4

CLINICAL PRESENTATION
Zoster rash is usually unilateral and does not cross the midline and erupts on adjacent dermatomes, and thoracic, cervical, and ophthalmic locations are the most common areas. The 7- to 10-day rash begins as erythematous and maculopapular rash with clusters of clear vesicles, which contain VZV. Vesicles progress to pustular, ulcer, and crust. Healing usually occurs in 2 to 4 weeks. Resulting pigmentation and scarring may be permanent, and partic-

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THE VACCINE
The licensed zoster vaccine in the United States is Zostavax (Merck & Co Inc, West Point, PA), which is a lyophilized preparation of the Oka/Merck strain of live attenuated VZV—the same strain used in the varicella vaccines Varivax and Proquad (Merck Vaccines, West Point, PA).4 Originally approved in 2006 for adults age 60 and older, the FDA approved Zostavax to prevent shingles for persons between age 50 to 59 on March 24, 2011. (Available at http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm248390.htm. Accessed September 20, 2011.) Persons who report a previous zoster event or with a chronic condition such as chronic renal failure, diabetes mellitus, pulmonary disease, or rheumatoid arthritis can receive the vaccine unless the person has conditions that are contraindicated.4 (See package insert for specific prescribing information. Available at: http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM132831.pdf. Accessed September 20, 2011).

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To prevent medication errors, store zoster The long-term efficacy of the zoster vaccine was tested in a double-blind phase 3 randomized placebo-controlled vaccine trial of 38,546 healthy adults aged 60 years and older with a history of varicella or 30 years of residency in the United States (a marker used for previous infection). Persons with history of zoster, allergy to vaccine components, evidence of decreased immunity, chronic pain, lack of mobility, hearing loss, or dermatologic disorders were excluded from the study. After randomization to receive zoster vaccine or placebo, subjects were followed for 3.1 years by monthly telephone calls and a close out interview. Ninety percent of the participants had at least 1 chronic medical condition.4,5

The 957 zoster cases were confirmed by PCR testing and followed for at least 182 days to assess outcomes. For vaccine recipients, 315 cases of zoster occurred and 642 occurred in the placebo group. Antiviral treatment within 72 hours of rash onset was 64.1% for the vaccine group and 65.9 for the placebo group.4,5

Study findings revealed that the vaccine reduced the risk for development of zoster by 51.3% and was 66.5% efficacious in preventing PHN. Furthermore, the vaccine reduced PHN severity in patients who developed zoster. Scarring, bacterial superinfection, palsies, and ocular and visceral complications were not significantly affected. Prevention of zoster was highest for the 60- to 69-year age category. Although effectiveness declined with age, an independent effect was noted in persons aged 70 to 79 years in reduction of PHN. Common adverse effects included injection site erythema, pain, and pruritis, which were usually mild.4,5

**PRACTICE IMPLICATIONS**

One in 3 persons will develop zoster during his/her lifetime. Death is uncommon, and about 3% require hospitalization.4 To prevent medication errors, store zoster and varicella vaccines separately and prepare only at the time of vaccination. In rare cases, persons develop a varicella-like rash after vaccination. If the person has close contact with persons at risk for varicella, contact precautions should be used although transmission of VZV following vaccination is rare and less common following zoster vaccination than following varicella vaccination.4 The long-term efficacy of the vaccine seems favorable.7

Any adverse events should be reported to the Vaccine Adverse Event Reporting System at http://www.vaers.hhs.gov or by telephone at 1-800-822-7967. Updated information regarding shingles, PHN, and zoster vaccine can be found at http://www.cdc.gov/vaccines/vpd-vac/shingles/default.htm. Valuable print resources for patients that describe who should and should not receive the vaccine, vaccine safety, and information regarding Medicare Plan reimbursement can be found at www.cdc.gov/vaccines. Vaccine information statements (VIS) can be obtained at http://www.cdc.gov/vaccines/pubs/vis/default.htm. This Web site also provides directions on how to download the VIS to mobile device, as well as information regarding new, existing, and future VIS resources.

Comprehensive information for clinicians and researchers can be found in the text of *Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis*, which is available on the Web at the National Library of Medicine Bookshelf at http://www.ncbi.nlm.nih.gov/books/NBK47376/.10 This valuable resource also describes related viruses such as human simplex type 1 and 2, Epstein-Barr virus, Kaposi’s sarcoma-associated herpesvirus, cytomegalovirus, and the varicella-zoster virus. Finally, Merck has valuable information for patient education available at http://www.zostavax.com/ and prescribing information can be accessed at http://www.merckvaccines.com/Products/zostavax/Pages/zostavaxhome.aspx.

**References**