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OREGON PUBLIC HEALTH DIVISION • DEPARTMENT OF HUMAN SERVICES

HOPE FOR HERPES ZOSTER

"Herpes zoster is fascinating because it arrives unpredictably, is readily diagnosed—a rare pleasure for most of us—and is difficult to explain."

R. Edgar Hope-Simpson, MRCS
Proceedings of the Royal Society of Medicine, 1965

This issue of *CD Summary* recapitulates the recently published Advisory Committee on Immunization Practices (ACIP) recommendations for preventing herpes zoster (i.e., shingles) with live attenuated varicella zoster virus (VZV) vaccine.[1] On May 25, 2006, the zoster vaccine was approved by FDA for persons ≥ 60 years of age and promises to save a lot of pain and suffering.

The relationship of zoster to varicella was discovered in the 19th century, and the theory that zoster is due to reactivation of dormant virus was advanced in 1965. Dr. Hope-Simpson's seminal longitudinal zoster studies found attack rates of 3 per 1000 per annum, increasing with age; disease severity increasing with age; non-seasonality; the absence of epidemic waves; and the association of high zoster prevalence with low varicella prevalence.[2] These study results have been reaffirmed in different settings with different study designs, including a 1997–2002 study among Washington and Oregon Kaiser Permanente Northwest Health Plan members.[3]

Dr. Hope-Simpson hypothesized that a critical level of VZV antibody was necessary to "blanket the explosion" of latent VZV which, when unsuppressed, can cause "fierce neuritis and neuralgias" in its victims and varicella in their contacts. Antibody decline could be reversed and the latent period prolonged by contact with varicella cases or by subclinical reactivation of VZV.[1, 2] Progressive age-related decline in VZV cell-mediated immunity is now thought to allow viral reactivation in aging but otherwise healthy individuals.[4]

Before the U.S. introduction of the varicella vaccine in 1995, nearly everyone had had varicella by age 30. Only 10%–30% of VZV-infected persons, however, developed zoster,[5] with those at lowest risk being persons repeatedly exposed to varicella or simply to children.[6] Widespread childhood varicella vaccination in the U.S. has had a big impact on varicella incidence—75%–80% incidence reductions have been reported (figure)—raising concern that zoster incidence might increase as VZV circulation decreases.[7, 8]

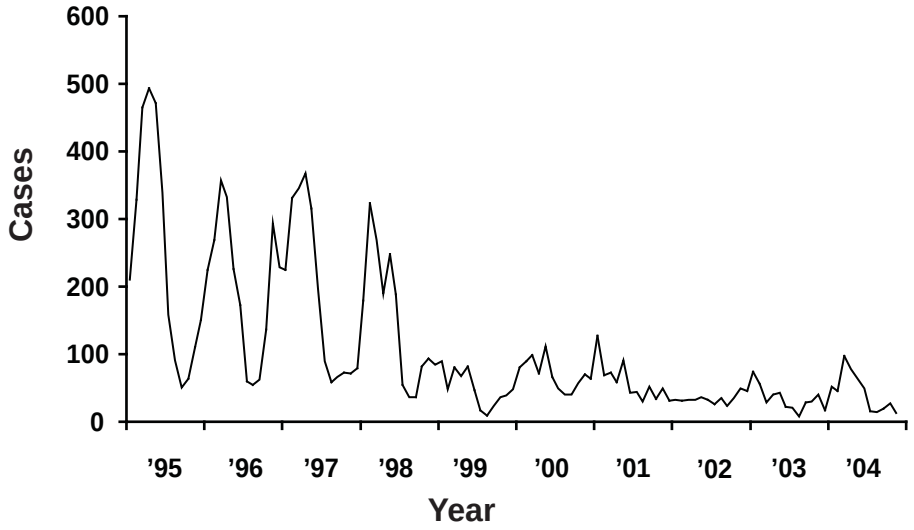
This is an unhappy scenario given that the pain and discomfort of zoster can diminish quality of life and ability to work to a degree comparable to conditions such as congestive heart failure and major depression,[9] and that post-zoster "fierce neuritis and neuralgias" may persist for years.[10] The estimated prevalence of this postherpetic neuralgia (PHN, pain persisting ≥ 30 days after rash resolves) is 500,000–1,000,000 cases in the United States; estimates of PHN proportions of zoster cases vary from 18%–30% 30 days after rash resolves to 10%–12% 90 days after rash resolves.[1] PHN can permanently damage central and peripheral nerves.[2]

In addition to PHN, 10%–25% of zoster cases get herpes zoster ophthalmicus which has complications of its own (corneal ulceration, retinitis, and glaucoma among others). In addition to opthalmic zoster, cases may get Ramsy-Hunt Syndrome (peripheral facial nerve palsy), Bell's Palsy, diaphramatic paralysis, Guillian-Barré Syndrome, and disfiguring facial scarring. A vaccine to prevent such disabling conditions is most welcome.

THE ZOSTER VACCINE TRIAL

The zoster vaccine trial, a Department of Veterans Affairs cooperative study known as the "Shingles Prevention Study", tested the hypothesis that immunization of older adults with live, attenuated VZV vaccine would boost their waning VZV cell mediated immunity and protect against zoster and PHN.[11] The study was a randomized, double-blind, placebo-controlled, multi-center trial of a

Varicella cases by month, Antelope Valley, California, 1995–2004



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live, attenuated "zoster vaccine" of a potency 14 times that of the currently licensed varicella vaccine (median 24,600 vs. 1350 plaque-forming units [PFU] of Oka/Merck VZV).

The trials took place between November 1998 and September 2001 with 38,546 adults over 60 with varicella histories; about 7000 subjects participated in a vaccine safety evaluation nested in the trial. Subjects with rash or unilateral pain saw doctors at their study site and completed *Zoster Brief Pain Inventories* (an assessment tool designed for this study) for six months following a diagnosis of "suspected herpes zoster". At the end of the study, before unblinding, suspected herpes zoster was confirmed (or not) using an algorithm that incorporated the results of PCR assay, virus isolation, and consensus clinical diagnosis of a five-physician panel.

Zoster vaccination reduced overall zoster incidence by 51%, post-herpetic neuralgia by 65%, and burden of illness (a severity-by-duration measure of the total pain and discomfort associated with zoster) by 61%. The vaccine had low rates of serious adverse events and systemic adverse reactions. The fact that no vaccine virus DNA was detected in suspected or confirmed cases indicated that the vaccine neither caused nor induced zoster.

ACIP RECOMMENDATIONS

ACIP recommends routine 1-dose zoster vaccination for individuals ≥ 60 years of age. Zoster vaccine is as fastidious as its progenitor, varicella vaccine, with respect to storage (freeze at ≤5°F/≤-15°C) and reconstitution (thaw and store at room temperature no longer than 30 minutes before administration). Administer zoster vaccine as a single 0.65-mL subcutaneous shot in the deltoid using syringes that don't contain anti-viral agents (preservatives, antiseptics, and detergents). Zoster vaccine can be administered simultaneously (though not from the same syringe or at the same site) with influenza, Td, Tdap, and pneumococcal polysaccharide vaccines.

Zoster vaccine is not licensed for persons aged <60 years and is not recommended for varicella vaccine recipients (the group of varicella vaccinees aged ≥60 years is extremely small and will remain so for at least a decade). Persons with a reported history of zoster may be vaccinated; there is no need to inquire about past varicella (this group is extremely large and will remain so for decades).

Contraindications to vaccination are allergy to vaccine components, primary or acquired immunodeficiency (bone marrow and lymphatic malignancies), AIDS and other manifestations of HIV (CD4+ T-lymphocytes of ≤200 mm² or ≤14% of total), immunosuppressive therapy, hemtopoietic stem cell transplantation, immune mediators and modifiers, and pregnancy (though pregnant women are unlikely to be in the target age group for vaccination).

Please refer to the ACIP recommendations for additional and more detailed information.[1]

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