Shingles Vaccination: What You Need to Know
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Shingles Vaccination: What You Need to Know

• The vaccine for shingles (Zostavax®) is recommended for use in people 60 years old and older to prevent shingles. The older a person is, the more severe the effects of shingles typically are, so all adults 60 years old or older should get the shingles vaccine.

• The shingles vaccine is specifically designed to protect people against shingles and will not protect people against other forms of herpes, such as genital herpes. The shingles vaccine is not recommended to treat active shingles or post-herpetic neuralgia (pain after the rash is gone) once it develops.

Varicella-Zoster Virus (VZV)

• Human alpha-herpesvirus
• Causes varicella (chickenpox) and herpes zoster (shingles)
• Primary VZV infection leads to varicella
• VZV establishes latency in dorsal root ganglia after primary infection
• VZV can reactivate at a later time, causing herpes zoster
• There are 3 licensed vaccines to prevent varicella (Varivax®, Proquad®) and herpes zoster (Zostavax®) in the US:
  — Varivax® (licensed 1995)
  — Proquad® (licensed 2005)
  — Zostavax® (licensed 2006)

Varicella: Clinical Features in Unvaccinated Cases

• Persons with varicella may develop prodrome of fever, malaise, headache, and abdominal pain 1-2 days before rash
• Rash involves 3 or more successive crops over several days; each crop usually progresses within less than 24 h from macules to papules, vesicles, pustules and crusts so that on any part of the body there are lesions in different stages of development
• Rash usually starts on face and trunk, then spreads to extremities
• Rash usually involves 250-500 lesions that are pruritic
• Lesions are typically crusted 4-7 days after rash onset

Varicella: Clinical Features in Vaccinated Persons (“breakthrough varicella”)

• Breakthrough varicella is defined as infection with wild-type varicella disease occurring > 42 days after vaccination
• Approximately 15-20% of 1-dose vaccinated persons may develop varicella if exposed to VZV
• Usually milder clinical presentation than varicella in unvaccinated cases
  — Usually low or no fever
  — Develop < 50 lesions
  — Experience shorter duration of illness
  — Rash predominantly maculopapular rather than vesicular
• 25-30% of breakthrough varicella cases are not mild and have clinical features more similar to varicella in unvaccinated persons

References:
CDC. Prevention of Varicella. MMWR 2007; 56(No. RR-4); Arvin A. Clin Microb Rev 1996; Vaccine 5th Edition

Varicella: Transmission

- Transmitted person to person by direct contact, inhalation of aerosols from vesicular fluid of skin lesions of acute varicella or zoster, or aerosolized respiratory tract secretions
- Average incubation period: 14-16 days after exposure to rash (range: 10-21 days)
- Period of contagiousness: 1-2 days before rash onset until all lesions crusted or disappear if maculopapular rash (typically 4-7 days)
- Varicella in unvaccinated persons is highly contagious (61-100% secondary household attack rate)
- Varicella in 1 dose-vaccinated persons 1/2 as contagious as unvaccinated cases
  - One study indicated that varicella in 1-dose vaccinees with < 50 lesions was 1/3 as contagious as unvaccinated persons although contagiousness in vaccinees with ≥ 50 lesions was similar to unvaccinated persons

Current Varicella Vaccination Policy in the United States

Implemented routine 2-dose childhood varicella vaccination program in 2C:
- 1st dose at age 12-15 months
- 2nd dose at age 4-6 years
- Catch-up vaccination of childre adolescents who had previously received one dose
  - 2 doses for all adolescents and adults without evidence of immunity
- Pre-natal screening and post-partum vaccination

Criteria for Determining Persons Who Can Be Considered Immune to Varicella

- Documentation of age-appropriate vaccination with varicella vaccine
- Laboratory evidence of immunity† or laboratory confirmation of disease
- Birth in the US before 1980§
- Diagnosis or verification of history of varicella disease by a health-care provider
- Diagnosis or verification of history of herpes zoster by a health-care provider

†Commercial assays may lack sensitivity for detecting vaccine-induced immunity
§For healthcare personnel, pregnant women, and immunocompromised persons, birth before 1980 should not be considered evidence of immunity

Contra-indications and Precautions for Varicella Vaccination

- Severe allergic reaction to vaccine component or following a prior dose
- Immunosuppression
- Pregnancy
- Moderate or severe acute illness
- Recent blood product (due to potential inhibition of response to varicella vaccination)

Varicella Vaccination in Certain Groups of Immunocompromised Persons

- Varicella vaccine may be administered to persons with isolated humoral immunodeficiency
- Patients with leukemia, lymphoma, or other malignancies whose disease is in remission and chemotherapy have been terminated ≥ 3 months can receive live-virus vaccines
- Consider varicella vaccination for HIV-infected children with CD4+ T-lymphocyte percentage of 15% or higher
  - Eligible children should receive 2 doses of single-antigen varicella vaccine 3 months apart
- Data on use of varicella vaccine in HIV-infected adolescents and adults lacking, but safety is likely to be similar to response in HIV-infected children. Vaccination may be considered for HIV-infected persons with CD4+T-lymphocyte count ≥ 200 cells/μl

Post-exposure Prophylaxis

- Varicella vaccine recommended for use in healthy persons without evidence of immunity within 3-5 days after exposure to varicella
  - ≥ 90% effective in preventing varicella if vaccinated within 3 days of exposure and ~ 70% effective in preventing varicella and ~100% effective in modifying severe disease if given within 5 days
  - Vaccination still recommended for those with no other evidence of immunity even after 5 days of exposure because it will help provide protection against future exposures
- Varicella Zoster Immune Globulin (available product, VarizIG™) recommended for certain groups at high risk for severe disease within 96 hours after exposure
Varicella Vaccine Storage and Handling

Varivax
- Store frozen at 5°C (-15°C) or colder at all times
- May be stored up to 72 hours at 35-46°F (2-8°C), but discard unused vaccine after 72 hours at this temperature
- Discard if not used within 30 min of reconstitution
- Store diluent at room temp or in refrigerator

MMRV
- Store frozen at 5°C (-15°C) or colder at all times
- May NOT be stored at refrigerator temperature AT ANY TIME
- Discard if not used within 30 min of reconstitution
- Store diluent at room temp or in refrigerator

Freezer Requirements for Varicella Vaccine Storage

- Acceptable Freezer Units:
  - Stand-alone freezers
  - Freezer compartments of refrigerator-freezer combinations, provided that the freezer compartment has its own separate, sealed, and insulated exterior door
- Unacceptable Freezer Units:
  - Units with an internal freezer door that is unsealed and un-insulated (e.g., small, dormitory-style refrigerators)
- Temperatures should be documented at beginning and end of each day

Varicella Vaccination of Healthcare Personnel

- To prevent disease and nosocomial spread of VZV, healthcare institutions should ensure that all HCP have evidence of immunity to varicella
  - Evidence of immunity = (1) laboratory evidence of immunity, (2) history of clinician diagnosed or verified varicella or zoster, (3) Documentation of age-appropriate vaccination
- Pre-vaccination serologic probably cost-effective
- Routine testing for varicella immunity after 2 doses of vaccine not recommended
  - Sensitive tests indicate 94-99% adults develop antibodies after second dose
  - VZV-specific cell-mediated immunity affords protection to vaccinated adults, even in the absence of detectable antibody response.
  - Available commercial assays may not be able to detect vaccine-induced immunity

Herpes Zoster: Clinical Description
Herpes Zoster (Shingles)

- Following initial infection (varicella), VZV establishes permanent latent infection in dorsal root and cranial nerve ganglia
- Years to decades later VZV reactivates and spreads to skin through peripheral nerves causing pain and a unilateral vesicular rash in a dermatomal distribution
- ~1 million cases in the U.S. annually
- Lifetime risk of developing zoster: about 30%

Clinical Features of Herpes Zoster

Prodrome: headache, photophobia, malaise, fever, abnormal skin sensations and pain

Rash:
- Unilateral, involving 1-3 adjacent dermatomes
- Thoracic, cervical, ophthalmic involvement most common
- Initially erythematous, maculopapular
- Vesicles form over several days, then crust over
- Full resolution in 2-4 weeks
- Occasionally, rash never develops (zoster sine herpete)

Complications of Herpes Zoster

- Postherpetic Neuralgia (PHN)
  - Pain ≥ 30 days occurs in 18-30% of zoster cases
  - Mild to excruciating pain after resolution of rash
  - Constant, intermittent, or triggered by trivial stimuli
  - May persist weeks, months or occasionally years
  - Can disrupt sleep, mood, work, and activities of daily living and lead to social withdrawal and depression
  - Risk factors for PHN include age ≥ 50, severe pain before or after onset of rash, extensive rash, and trigeminal or ophthalmic distribution of rash

- Herpes Zoster Ophthalmicus
  - ~15% of HZ cases
  - Can occur when ophthalmic division of trigeminal nerve is involved
  - Untreated, 50-70% develop acute ocular complications
  - Can lead to chronic ocular complications, reduced vision, even blindness

- Neurologic complications
  - Myelitis, encephalitis, ventriculitis, meningoencephalitis, cranial nerve palsies, ischemic stroke syndrome

- VZV viremia
  - Cutaneous dissemination, pneumonia, hepatitis, disseminated intravascular coagulation

- Dermatologic complications
  - Secondary infections of rash
  - Permanent scarring and changes in pigmentation

VZV Transmission from Zoster

- VZV can be transmitted from persons with zoster to persons with no history of varicella disease or vaccine and cause varicella
- Risk of VZV transmission from zoster is much lower than from varicella
- Transmission is mainly through direct contact with zoster lesions, although airborne transmission has been reported in healthcare settings
- Localized zoster is only contagious after the rash erupts and until the lesions crust
- Transmission from localized zoster can be decreased by covering the lesions

Risk Factors for Herpes Zoster

- Increasing age
- Immunosuppression
  - Bone marrow and solid organ transplantation
  - Patients with hematological malignancies and solid tumors
  - HIV
  - Immunosuppressive medications
- Gender: Increased risk in females
- Race: Risk in blacks less than half that in whites
- Trauma or surgery in affected dermatome
- Early varicella (in utero, infancy): Increased risk of pediatric zoster

[Graph showing incidence rates per 1000 per year across age groups with labels: HZ: N=321, PHN: N=46]


Herpes Zoster Vaccination Coverage:
U.S., Age 60 or Older, 2007-2009

[Graph showing percentage of vaccination coverage across years]

Herpes Zoster Vaccine

- Licensed in 1996
- Live, attenuated VZV
- Same strain used in the varicella vaccine, but 14x more potent
- Administered subcutaneously in deltoid region

HERPES ZOSTER: VACCINE INFORMATION

Herpes Zoster Vaccine Efficacy

- Decreased zoster incidence by 51%
- Decreased risk of post-herpetic neuralgia in all participants by 67%
- Decreased burden of illness (severity x duration) in all participants by 61%

Omen NEMI 2005

Disease Protection

- In a clinical trial involving thousands of adults 60 years old or older, Zostavax reduced the risk of shingles by about half (51%) and the risk of post-herpetic neuralgia by 67%. While the vaccine was most effective in people 60-69 years old it also provided some protection for older groups.
- Research suggests that the shingles vaccine is effective for at least six years, but may last much longer. Ongoing studies are being conducted to determine exactly how long the vaccine protects against shingles.
Who Should Get the Vaccine

- CDC recommends Zostavax for use in people 60 years old and older to prevent shingles. This is a one-time vaccination. There is no maximum age for getting the shingles vaccine.
- Anyone 60 years of age or older should get the shingles vaccine, regardless of whether they recall having had chickenpox or not.
  - Studies show that more than 99% of Americans ages 40 and older have had chickenpox.

Who Should Get the Vaccine 2

- At this time, CDC does not have a recommendation for routine use of shingles vaccine in persons 50 through 59 years old. However, the vaccine is approved by FDA for people 50 and older.
- It is available by prescription from a health care provider.

Who Should Get the Vaccine 3

- Even if you have had shingles, you can still receive the shingles vaccine to help prevent future occurrences of the disease.
- There is no specific time that you must wait after having shingles before receiving the shingles vaccine.
- Generally, a person should make sure that the shingles rash has disappeared before getting vaccinated.

ACIP Recommendations for Zoster Vaccine

- In October 2008, the Advisory Committee on Immunization Practices (ACIP) recommended a dose of the herpes zoster vaccine (HZV) for all adults ≥60 years of age unless they have contraindications.
- HZV should be offered at the patient’s first available clinical encounter.


The Sticky Wicket of HZV

- The phrase comes from the game of cricket. The pitch (that is, the ‘field of play’ in cricket) is also known as "the wicket". It can be affected by rain and the sun, causing the ball to bounce unpredictably: a pitch which had been wet would become increasingly difficult to bat on, as it dried out.
- Such a pitch was referred to as a "sticky wicket" for a batsman because the ball's bounces are unpredictable. Such wickets are far less common in cricket since matches stopped being played on uncovered pitches.

Impact of Age on Burden of HZ: Key Observation

- Not only is the entire adult US population infected with varicella and thus at risk of HZ the rest of their lives, but the burden of HZ disease actually increases greatly in the latter half of life, decade by decade.
- Very different pattern than most other vaccine preventable diseases for which peak risk period is self-limited or declines to low levels in the latter half of life, decade by decade.
Impact of Age on Burden of HZ

Burden of HZ increases sharply after age 50
- Incidence of HZ itself increases with age
- Given occurrence of HZ, the following increase with age:
  - Proportion of HZ with non-pain complications
  - Proportion of HZ hospitalized (also length of stay and cost)
  - Proportion of HZ associated with death
  - Interference with activities of daily living (ADLs)
  - Proportion of HZ with acute pain, and progressing to PHN
    - Given PHN, the following increase with age:
      * Severity and duration of pain
      * Tolerating PHN: impact of age on vulnerability
- Exception: work-loss for HZ declines with age (retirement)

HZ Incidence by Age: U.S., 2000-1*

PHN Rate in Population, by Age: Olmsted County, 1996-2001*

HZV Duration of Protection: A Key Unknown
- Short Term Persistence Study (STPS): What we know: it is clear HZV protects 3-4 years and perhaps a few years longer
- What we don’t know: will HZV protect 15 years or 30 years when it really counts?
  - In projecting forward decades, it is much easier for data to prove that waning is occurring than to disprove it
- Long Term Persistence Study (LTTPS)
  - Will extend STPS several years (results within the year)
  - Logistic controls (adjusting for secular changes in HZ rates)
  - Immunogenicity: no good serologic or CMI correlates
  - Follow up observational studies will be important in time

HZV Duration of Protection: VE_HZ*

How Long Does HZV Need to Protect? *

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* http://www.cdc.gov/ncidod/ID/STATS/tables.html
Life expectancy expected to increase for all age states ~1yr over coming 20 yrs
ACIP Recommendations for Zoster Vaccine

- HZV can be administered simultaneously with influenza and pneumococcal vaccines
- HZV is recommended whether or not the patient reports a prior episode of zoster
- It is not necessary to check varicella history or titers before administering HZV
- HZV should be offered to eligible persons including those >80 y.o., frail, or with chronic illnesses


Who Should NOT Get the Vaccine 1

- A person who has ever had a life-threatening or severe allergic reaction to gelatin, the antibiotic neomycin, or any other component of shingles vaccine. Tell your doctor if you have any severe allergies.
- Women who are or might be pregnant
Contraindications for Zoster Vaccine

- Immunosuppression (high-dose steroids, biological response modifiers, chemotherapy, AIDS) is a contraindication for HZV
- HIV-positive status alone is not an contraindication
- Persons ≥60 y.o. anticipating immunodeficiency due to initiation of treatments or progression of illness should be offered HZV
- HZV is not recommended for persons ≥60 y.o. who have received the varicella vaccine


Side Effects 1

- The vaccine has been tested in about 20,000 people aged 60 years old and older.
- No serious problems have been identified with shingles vaccine.
  - The most common side effects in people who got the vaccine were redness, soreness, swelling or itching at the shot site, and headache.
- The shingles vaccine does not contain thimerosal (a preservative containing mercury).

Side Effects 2

- There is no documentation of a person getting chickenpox from someone who has received the shingles vaccine, which contains varicella zoster virus.
  - It is safe to be around infants and young children, pregnant women, or people with weakened immune systems after you get the shingles vaccine.
  - Some people who get the shingles vaccine will develop a chickenpox-like rash near the place where they were vaccinated. As a precaution, this rash should be covered until it disappears.

Adult Immunization Resources

For Clinicians

- ACP Adult Immunization Initiative
  http://www.acponline.org/clinical_information/resources/adult_immunization/
- AAFP Vaccines & Immunizations
- ACOG
  http://www.immunizationforwomen.org/resources/acog_resources

For Public Health Professionals

- Campaign for AI
  http://www.adultvaccination.org/professional-resources
- National AI Summit
  http://www.preventinfluenza.org/NAIS_slides_2012.asp
- CDC
  http://www.cdc.gov/vaccines/schedules/hcp/adults.htm
- NACCHO
  http://www.naccho.org/topics/HPDP/immunization/
Resources - HZV

- Best Q&A Site: http://www.immunize.org/askexperts/experts_zos.asp
- Best Discussion of Cost-Benefit of Early Vaccination: Harpez Slides for June 20, 2011 ACIP – No longer on site, but can be requested.
- ACP Adult Immunization Portal http://immunization.acponline.org/index.html

Adult Immunization Resources

For The Public

- ACP http://www.acponline.org/patients_families/immunization/
- CDC http://www.cdc.gov/vaccines/special-groups/adults.htm
- CDC You Call The Shots http://www.cdc.gov/vaccines/ed/youcalltheshots.htm
- Campaign for AI http://www.adultvaccination.org/

For the ‘Device’ Savvy

- “Shots by STFM” for your Mobile Device and Smartphone
- ACP Immunization Advisor
  Search by age or underlying medical circumstance, browse the Vaccine Library to determine the vaccines their adult patients need. Immunization news and updates from ACP immediately available from within the app. http://immunization.acponline.org/app/

Contact Info

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Appendix 1
Reimbursement for Vaccination

Stop, your making my head hurt!
Appendix 2
Immunization Action Coalition
Q&A’s 2012
http://www.immunize.org/askexpert/s/experts_zos.asp

Immunization Action Coalition Q&A’s 2012

• Q: What do you think about giving zoster vaccine to nursing home patients? Should healthcare personnel in nursing homes be tested to see if they have had chickenpox before taking care of someone who has received zoster vaccine?

• A: Zoster vaccine can be administered to anyone age 60 years and older regardless of where they reside, unless they have a contraindication to vaccination. All healthcare personnel should ensure they are immune to varicella regardless of the setting in which they work and regardless of their patients’ receipt of zoster vaccine.

• Q: The Zostavax vaccine (Merck) package insert says that Zostavax should not be given simultaneously with pneumococcal polysaccharide vaccine (PPSV). What does ACIP say about this?

• A: ACIP has not changed its recommendation on the simultaneous administration of these two vaccines (i.e., they can be given at the same time or any time before or after each other).
Q: Can I give long-term care residents zoster, injectable influenza, and pneumococcal vaccines on the same day?
A: Yes. Here are the general rules: (1) all vaccines used for routine vaccination in the United States can be given on the same day; (2) an inactivated vaccine can be administered either on the same day as or at any time before or after another inactivated or a live vaccine; and (3) any 2 LIVE vaccines that are not given on the same day must be spaced at least 4 weeks apart.

Q: Is there an upper age limit for receipt of the zoster vaccine? Local providers are reluctant to give zoster vaccine to persons age 80-plus years.
A: There is no upper age limit for zoster vaccine. The incidence of herpes zoster increases with age. It is known that about 50% of persons living until age 85 years will develop zoster.

Q: In March 2011, FDA expanded the age indication for Zostavax to include the vaccine’s use in people age 50 through 59 years (while retaining the age indication for use in people age 60 years and older). What does ACIP recommends about this?
A: At its June 2011 meeting, the ACIP reviewed the current status of ZOS licensure and the burden of herpes zoster (HZ) disease. ACIP declined to vote to expand the recommendations for the use of ZOS to include people age 50 through 59 years for the following reasons:

- vaccines that contain varicella virus (i.e., varicella, ZOS, and MMRV vaccines) are in recurrent short supply in the U.S.,
- though the burden of HZ disease increases after age 50, disease rates are lower in this age group than they are in the 60-years-and-older age group,
- currently, ZOS vaccination rates are less than 10 percent, and
- a recommendation to vaccinate people age 50–59 years could result in more zoster disease if the limited supply of vaccine were to be given to people whose risk of disease is lower than that of older, more vulnerable adults.

Q: I understand that Varivax, ProQuad, and Zostavax each have different concentrations of antigen. Would you tell me how they are different?
A dose of Varivax has 1,350 plaque forming units (PFUs), ProQuad contains 9,800 PFUs (7 times higher than Varivax), and Zostavax contains 19,400 PFUs (14 times higher than Varivax).

Q: We accidentally gave a 47-year-old healthcare worker Zostavax instead of Varivax for work. Does this count?
A: Yes, but this is a serious vaccine administration error because Zostavax vaccine contains about 14 times as much varicella vaccine virus as Varivax.
- You should document the event and establish procedures to prevent this from happening again.
- The dose of zoster vaccine can be counted as the first of two doses of varicella vaccine for an adult who is not immune to varicella. The second dose of varicella vaccine should be given 4 to 8 weeks after the first dose.
Q: A 60-year-old patient was given varicella vaccine instead of zoster vaccine. Should the patient still be given the zoster vaccine? If so, how long an interval should occur between the 2 doses?

A: "If a provider mistakenly administers varicella vaccine to a person for whom zoster vaccine is indicated, no specific safety concerns exist, but the dose should not be considered valid and the patient should be administered a dose of zoster vaccine during that same visit. If the error is not immediately detected, a dose of zoster vaccine should be administered as soon as possible but not within 28 days of the varicella vaccine dose to prevent potential interference of 2 doses of live attenuated virus."