GLOBAL HEALTH PRESS

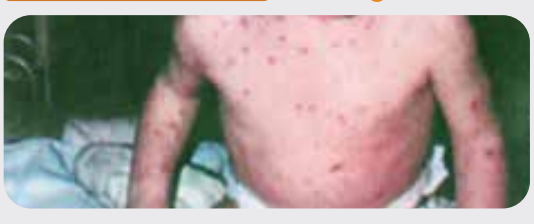
# VARICELLA AND ZOSTER (SHINGLES)

## What are VZV-associated diseases?

**Varicella-Zoster Virus (VZV) causes two major illnesses:**

- Primary infection as varicella (chickenpox) and reactivation as herpes zoster (shingles).
- After varicella, VZV establishes lifelong latency in sensory neurons; about 30% of people will develop zoster during their lifetime, with risk rising after age 50 and in immuno-compromised hosts. Zoster can lead to complications such as post-herpetic neuralgia (PHN), ophthalmic disease, neurological involvement, disseminated infection, and increased cardiovascular events.

## Microbiology



Effective control of VZV depends mainly on cell-mediated immunity (CMI); waning CMI with age or immunosuppression predisposes to zoster and PHN. Humoral antibodies prevent reinfection and limit virus spreads but are less critical for resolving disease or preventing reactivation.

Vaccines (live varicella vaccine, live zoster vaccine, and recombinant zoster vaccine) boost VZV-specific CMI, which correlates with protection against zoster.

## Pathogenesis

VZV is a human alpha-herpesvirus transmitted primarily via airborne spread of virus from skin lesions of varicella or zoster. Primary infection involves respiratory mucosa, lymphoid tissue, viremia, and a generalized vesicular rash; latent infection is established in sensory ganglia with restricted viral gene expression.

Reactivation occurs when VZV resumes replication in neurons with anterograde spread to skin, typically causing a unilateral dermatomal vesicular eruption.

## Epidemiology

Before universal vaccination, most varicella occurred in childhood, with high household secondary-attack rates and substantial hospitalization and complications.

Two-dose childhood varicella vaccination markedly reduces incidence and severe disease; long-term follow-up in China shows around 90% effectiveness against any varicella and very low breakthrough rates with a 2dose schedule.

Zoster incidence increases sharply with age and in immunocompromised adults. E.g. in rheumatoid arthritis and SLE zoster risk increases several-fold, especially under immunosuppressive therapy.

## Transmission

VZV spreads mainly via airborne droplets from skin lesions of varicella or zoster and, less commonly, via direct contact with vesicular fluid.

Vricella is highly contagious; in households, about 80% of susceptible contacts become infected after exposure to a case.

Zoster lesions can transmit VZV to susceptible individuals, leading to varicella rather than zoster, emphasizing infection control and vaccination.

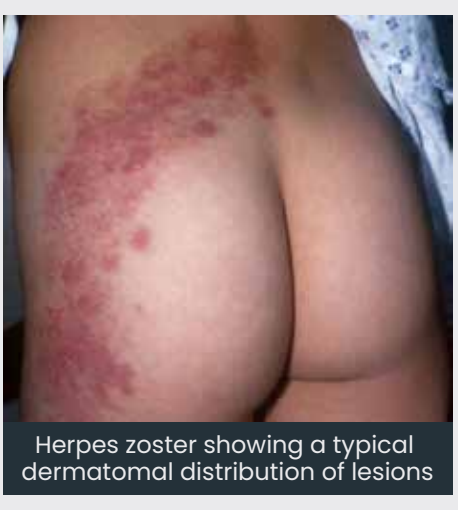
## Clinical disease

In immunocompetent children, varicella usually causes a self-limited febrile vesicular rash lasting about a week. Complications include bacterial superinfection, pneumonia, and rarely CNS disease or activation of the clotting system with bleedings and stroke.

Zoster presents with dermatomal pain and unilateral vesicular rash; complications include PHN, ocular disease, neurological involvement, and disseminated infection, especially in older or immunocompromised adults. Antivirals (e.g., acyclovir, valacyclovir, famciclovir) started within 72 hours of rash onset reduce viral replication and speed healing.

Early-stage varicella in a healthy child

Mucosal varicella in a child with leukemia



Herpes zoster showing a typical dermatomal distribution of lesions

## Prevention in general

**Prevention strategies include:**

- Routine childhood varicella vaccination with 2 doses to reduce primary infection and circulating virus.
- Adult zoster vaccination to prevent reactivation, reduce zoster incidence, and lower risk of PHN and other complications.
- Prompt antiviral treatment of varicella and zoster in high-risk patients and infection-control measures around cases.

## Vaccines

- **Live attenuated varicella vaccine (Oka strain)**
  - Developed in the 1970s; used globally for childhood immunization and in some combination MMRV products.
  - Vaccine strain may cause zoster as well, but milder and at a log fold lower rate than natural infection.
  - One dose protects about 85% of children against any varicella and nearly 100% against severe disease; two doses increase effectiveness to about 98%.
  - Breakthrough disease after 2 doses is usually mild but remains transmissible, so high coverage is important.
- **Live attenuated zoster vaccine (Zostavax, no longer widely used)**
  - High-dose Oka-strain vaccine (~15× varicella dose) given as a single dose to older adults.
  - Provided about 50% protection against zoster and PHN in adults ≥60 years, with efficacy waning substantially over time (down to ~20% after ≥7–10 years).
- **Adjuvanted recombinant zoster vaccine (RZV, Shingrix)**
  - Non-live subunit vaccine containing VZV glycoprotein E plus AS01B adjuvant; administered as 2 intramuscular doses.
  - Phase 3 trials (ZOE50/70) showed ~97% efficacy against zosters in adults ≥50 years and ~90% in those ≥70 years, with similar high protection against PHN.
  - Long-term follow-up (ZOELTFU) shows vaccine efficacy ~80% against zoster and >85% against PHN up to ~11 years after vaccination, with sustained humoral and cellular responses and no new safety signals.
  - Real-world data in rheumatoid arthritis demonstrate ~16% relative reduction in zoster and ~40% reduction in all-cause mortality among RZV recipients versus unvaccinated RA patients, though mortality findings may partly reflect residual confounding.
  - In SLE, a randomized trial in Korea showed robust humoral (≈98% responders) and cellular responses with no increase in disease flares, despite frequent local and systemic reactogenicity.

**Table 1: Varicella vaccines used globally (examples)**

| Region / context | Brand (example) | Type / strain | Key points |
|---|---|---|---|
| North America, Europe | Varivax, Varilrix and similar | Live attenuated Oka-strain varicella vaccine | Widely used in routine childhood immunization; 1 dose ~85% effective, 2 doses ~98% effective against varicella, with major reductions in hospitalizations and deaths. |
| Asia (China, others) | Domestic Oka-derived vaccines | Live attenuated varicella vaccine | Two - dose schedules in China show high long - term effectiveness (~90% vs any varicella) with low breakthrough incidence in school-aged children. |
| Latin America, other regions | Various Oka-strain products, some MMRV combinations | Live attenuated varicella or MMRV | Used in national programs or private sector; impact similar where high two-dose coverage is achieved.VacciTUTOR-Chapter-41. |

**Table 2: Zoster vaccines: Key comparison**

| Feature | Zostavax (ZVL) | Shingrix (RZV) |
|---|---|---|
| Type | Live attenuated VZV (high-dose Oka strain) | Recombinant gE subunit with AS01B adjuvant |
| Manufacturer | Merck (MSD) | GSK |
| Antigen(s) | Whole live attenuated VZV at very high dose | Purified VZV glycoprotein E |
| Regimen | 1 dose, SC | 2 IM doses, 2–6 months apart (1–2 months in some immunocompromised adults) |
| Primary endpoint in pivotal trials | Confirmed herpes zoster and PHN in adults ≥60 years | Confirmed herpes zoster; PHN and other complications in adults ≥50 and ≥70 years |
| Efficacy/effectiveness (approx.) | ~50% against zoster and PHN in adults ≥60; marked waning to ~20% by 7–10 years. VacciTUTOR-Chapter-41 | ~97% against zoster in ≥50 and ~90% in ≥70 years over ~3–4 years; PHN ~90% protection.shingrix-1.pdf Long-term VE ~80% against zoster and >85% against PHN up to ~11 years; durable immune responses. |
| Current role | Largely replaced in many settings; no longer standard of care in US and several other countries. | Preferred zoster vaccine for immunocompetent and many immunocompromised adults in multiple guidelines; strong real-world effectiveness including in RA and transplant recipients. |

**Current CDC (USA) recommendations – please follow local guidelines**

- **Children – varicella vaccination**
- Routine 2dose series of live attenuated varicella vaccine for all children.
- First dose at age **12–15 months**, second dose at **4–6 years**; catch-up vaccination for older children and adolescents without evidence of immunity.
- **Adults – zoster vaccination (Shingrix)**
- **All adults ≥50 years:** 2 doses of recombinant zoster vaccine (RZV, Shingrix), 2–6 months apart, regardless of prior zoster, prior Zostavax, or varicella history.
- **Adults ≥19 years who are or will be immunodeficient or immunosuppressed:** 2-dose Shingrix series, with the second dose 1–2 months after the first in some immunocompromised groups.
- No current recommendation to use live zoster vaccine; RZV is the preferred product in CDC/ACIP guidance.

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