# Shingles

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## Abstract

Shingles, also known as herpes zoster, is characterised primarily by a painful, blistering skin rash caused by a reactivation of varicella zoster virus from its latent state within a person's body. It is commonly preceded by a unilateral burning pain, tingling sensation and skin tenderness. Postherpetic neuralgia is a common and debilitating complication of herpes zoster and can often impair the quality of life of the affected persons. This article provides a brief overview of shingles, including the clinical manifestations, management and prevention thereof.


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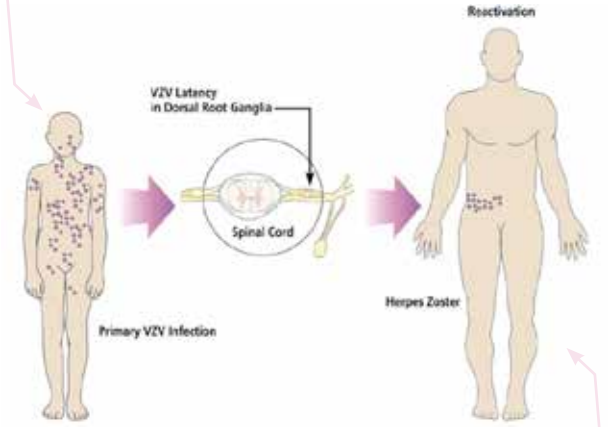
## Introduction

The herpesvirus family contains several important human viral pathogens. A characteristic property of herpesviruses is their ability to undergo periodic reactivation and to establish lifelong persistent infections in their hosts.[1] An example of such a virus is varicella-zoster virus (VZV) that causes two distinct clinical entities: varicella (chickenpox) and herpes zoster (shingles).[2] A child who has not been vaccinated against VZV will develop chickenpox (primary infection) after exposure to the virus either via the airborne route or direct contact with an infected person. The virus incubates for 15 days or more in the upper respiratory tract and can therefore be transmitted through coughing or sneezing. Varicella-zoster virus continues to spread to the bloodstream and migrates to the skin, giving rise to a characteristic **exanthematous vesicular rash**.[2,3] The virus infects dorsal route ganglia where it remains latent until reactivated.[2]

## Epidemiology and clinical manifestations

Humans are the only known reservoir for VZV.[2] Varicella is one of the classic childhood diseases and highly communicable with 90% of seronegative individuals being susceptible to the virus. The infectious stage is 48 hours prior to onset of the vesicular rash, during the period of vesicular formation (4–5 days), and until all vesicles have crusted over. Although primary varicella is an endemic disease affecting different races and genders equally, infection is more common in the winter and early spring. Children between the ages of 1–14 years are mostly affected with only 10% of the infections occurring above the age of 15 years.[2,4] Since the introduction of VZV vaccination, the incidence of these disease variants has significantly reduced.[2]

Exanthematous: characterised by or involving a widespread skin eruption or rash




Dermatomal: an area of skin that is supplied with the nerve fibres of a single, posterior, spinal root

**Figure 1.** Exanthematous *vs* dermatomal vesicular rash

Resource: http://jaoa.org/data/Journals/JAOA/932109/s2fig1.jpeg

Contrary to varicella, herpes zoster occurs sporadically and evenly throughout the year[2] with a lifetime risk of at least 32%.[5] A prerequisite for developing shingles (recurring infection) is an earlier exposure to VZV. The virus remains latent in the host for a considerable period of time, ranging from years to decades.[6] When reactivated, the virus travels down the affected nerve to the skin and presents with a **dermatomal vesicular rash**.

The virus does not spread to the bloodstream or lungs but active virus particles are contained within the shingles rash and can only

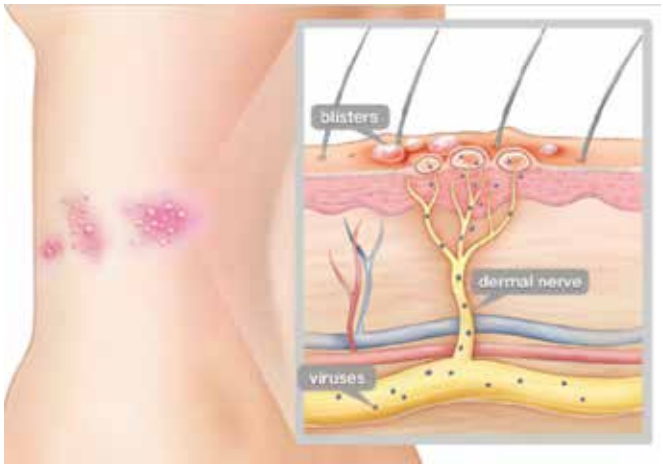



**Figure 2.** Shingles presents with a dermatomal vesicular rash

Resource: http://blog.urparamount.com/wp-content/uploads/2015/02/shingles_illustration.jpg

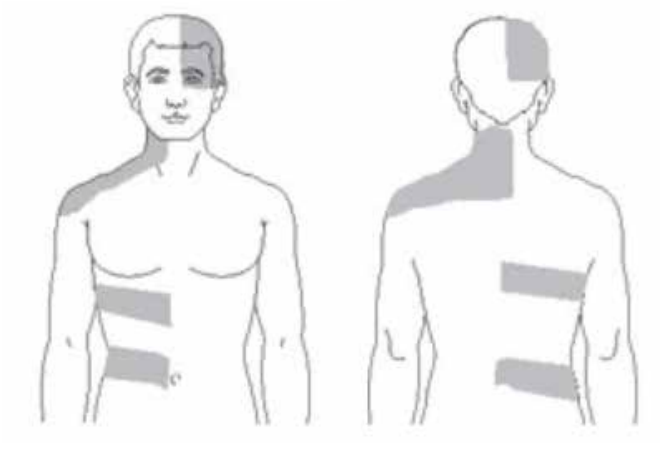


**Figure 3.** Dermatomal rash

Resource: https://www.cdc.gov/shingles/about/symptoms.html

spread via direct contact with the open blisters. If such a contact has never had chickenpox before or hasn't been vaccinated he/she will most likely continue to develop chickenpox, not shingles.[7]

When latent varicella-zoster virus becomes reactivated, it presents as an acute, cutaneous viral infection.[8] Although shingles can occur at any age, its incidence is highest among individuals in their sixth decade of life and beyond.[2] The increased incidence in the elderly is due to a decline in VZV host cell-mediated immunity function with a 50% chance of contracting the virus above the age of 50 years compared to a 20–30% chance in individuals younger than 50 years.[9] Other factors that decrease the function of the immune system include HIV, chemotherapy, malignancies, radiation and chronic corticosteroid use.[10] Immunocompromised persons are at increased risk with the reactivation of VZV occurring earlier in life and the disease process likely to be prolonged.[4] Zoster may disseminate in immunocompromised persons, causing generalised skin lesions and central nervous system, pulmonary, and hepatic involvement.[5]

## Signs and symptoms

Herpes zoster mainly affects a single dermatome of the skin,[4] and the dermatomes from T3 to L3 are most frequently involved.[2] Commonly affected areas include the lower cervical, thoracic and lumbar posterior root ganglia. A unilateral burning pain, tingling sensation and skin tenderness usually precedes the eruption.[2] Another commonly affected nerve is the trigeminal ganglion, mostly involving the ophthalmic branch (zoster opthalmicus). Haemorrhagic cystitis or urinary retention may be associated with the involvement of the sacral ganglia. Vesicles in the external auditory meatus are known as Ramsay-Hunt syndrome which is thought to be a form of zoster involving the seventh nerve.[4] The activation of VZV and subsequent destruction of neurons in the sensory ganglia and afferent peripheral nerves stimulates the inflammatory cascades which primarily result in the onset of excruciating pain that impacts on a patient's quality of life.[2] The general total duration of the disease is 7–10 days, but for the skin to return to normal can take as long as 2–4 weeks.[2]

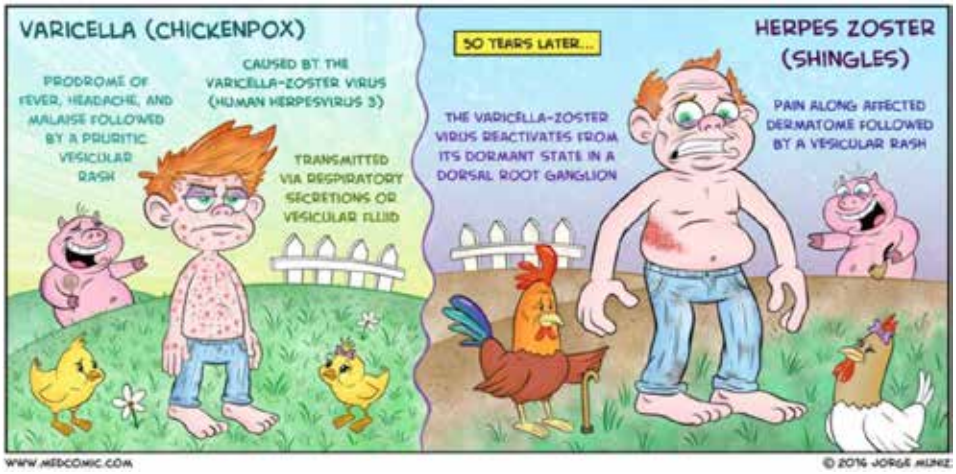



**Figure 4.** Varicella *vs* herpes zoster

Resource: https://i.pinimg.com/736x/f0/46/f4/f046f428368158f4d3aa0fa087975efc.jpg

## Postherpetic neuralgia

The most common and debilitating complication of herpes zoster is neuralgia. It is uncommon in young individuals, but affects at least 50% of zoster patients over the age of 50 years. The affected patients experience a persistent pain in the involved dermatome for months after the cutaneous infection has resolved.[2] Although postherpetic neuralgia (PHN) is a self-limiting condition,[10] and 80% of patients improve and recover over one year,[4] it can last indefinitely.[10,11]

## Management of shingles

Shingles is an acute neurologic disease that warrants immediate medical attention. The host's immune state together with the presentation of zoster, generally determines the therapeutic choices.[12] The three main treatment goals are:

1. timeous and appropriate treatment of the acute viral infection
2. effective pain management
3. prevention of PHN

In-patient care is not required for uncomplicated zoster, but hospital admission should be considered for the following persons[12]:

- severe symptoms
- immunocompromised
- atypical presentations e.g. myelitis
- involvement of more than two dermatomes
- significant facial bacterial superinfection
- disseminated herpes zoster
- ophthalmic involvement
- meningoencephalopathic involvement

Conservative therapy includes NSAIDs, wet dressing with 5% aluminium acetate (Burow's solution) applied 4–6 times per day for 30–60 minutes, and lotions, e.g. calamine.[12]

### *Antiviral agents*[10]

The first line of treatment is acyclovir, administered via the oral route. A major drawback of acyclovir is its dosing frequency (five times daily). Two other antiviral agents used as alternatives in the treatment of shingles are famciclovir and valacyclovir. Antivirals are most effective when administered within 72 hours after the rash has appeared. Furthermore, antiviral agents are only effective while new lesions are actively being formed – they are unlikely to be of any benefit once the blisters have crusted over.

Acyclovir is a DNA polymerase inhibitor and the prototype antiviral medicine. Valacyclovir is a prodrug of acyclovir, has a better bioavailability compared to the prototype, and a dosing interval of eight hours. Oral administration of valacyclovir produces blood medicine levels comparable to acyclovir administered via the IV route. Famciclovir has a better bioavailability when compared to both acyclovir and valacyclovir while having the same dosing frequency as the latter. All three antiviral agents are well tolerated in general, but common side-effects include nausea, headache, vomiting, dizziness and abdominal pain.

### *Corticosteroids*[10]

Multiple treatment approaches are often required to treat PHN effectively. To reduce the pain caused by shingles and the incidence of PHN, oral corticosteroid therapy provides modest benefits. Although the value of corticosteroid use in the management of shingles is debatable, it is commonly used. Prednisone in combination with antiviral agents reduces the pain associated with the disease – it decreases the degree of neuritis caused by active infection and possibly decreases residual damage to affected nerves. The use of corticosteroids is therefore justified, if not contraindicated.

### *Analgesics*[10]

Pain associated with shingles ranges from mild to excruciating and requires pain management. Depending on the severity of pain, patients can be managed with over-the-counter analgesics, although patients with severe pain may require opioids additionally. It is important that the patient takes the pain medication on a regular basis as it will result in better pain control and reduced anxiety.

### *Topical agents*[10]

Capsaicin, lidocaine patches and nerve blocks can be used in selected patients. Capsaicin, an extract from hot chili peppers, enhances the release of substance P from nerves and prevents its re-accumulation. Depletion of substance P from peripheral sensory nerves provides a rational basis for its use topically.[13] Capsaicin cream should be applied three to five times daily to the affected area. The following counselling points are important:

- regular application is important for continued benefit
- pain will increase during the first few days after initiation
- patients should wash their hands thoroughly after application

### *Tricyclic antidepressants*[10]

Tricyclic antidepressants (TCA) inhibit the reuptake of serotonin and norepinephrine and can be effective adjuncts to reduce the neuropathic pain of PHN. Commonly used agents include amitriptyline, nortriptyline, imipramine and desipramine, initiated at a low dose at bedtime. The dose is then titrated upwards until an effective dose is achieved. The effect is not immediate and a period of at least three months should be allowed to judge a patient's response. Anticholinergic side-effects to be expected range from sedation, dry mouth, postural hypotension, blurred vision and urinary retention. Cardiac conduction abnormalities are a concern with TCAs and should be taken into consideration in elderly patients and patients with cardiac disease or liver impairment.

### *Anticonvulsants*[10]

Phenytoin, carbamazepine and gabapentin are often used to control PHN and the different agents appear to be equally effective. A lack of response to one agent does not necessarily mean another won't be effective, and selection often involves trial and error. The required dosages to obtain effective pain relief are often lower than those used in the treatment of epilepsy.

## Vaccination against herpes zoster

Vaccination is an important intervention against herpes zoster and PHN since neither can be treated adequately with current

medication.[14] The zoster vaccine (Zostavax®) is a live attenuated virus vaccine indicated for the prevention of herpes zoster in persons of age 50 and older.[15] Herpes zoster vaccination reduced the burden of illness by 61.1%, the incidence of PHN by 66.5%, and the incidence of herpes zoster by 51.3%.[16] Although the ability of the vaccine to prevent VZV infection declined with age, the risk of PHN was lowered among the older vaccinated population who still developed herpes zoster.[14] Zostavax® is administered as a single dose, regardless of a previous history of zoster infection and without a need to screen for a history of varicella infection or to conduct laboratory testing for serologic evidence of prior varicella infection.[15]

The Advisory Committee for Immunisation Practices (ACIP) has developed recommendations and set standards on immunisation practices for adult vaccination and recommends routine immunisation with zoster vaccine in persons 60 years and older.[17]Although the vaccine is approved for use in persons 50 years and beyond, the ACIP does not recommend routine use of herpes zoster vaccine in people aged 50 to 59 years. Healthcare providers considering the herpes zoster vaccine for certain persons in this age range should discuss the risks *vs* benefits ratio with their patients.[17] Healthcare providers may consider administering the vaccine in patients aged 50 to 59 years depending on certain factors such as poor anticipated tolerance of herpes zoster or postherpetic neuralgia symptoms (e.g. attributable to pre-existing chronic pain, severe depression, or other comorbid conditions; inability to tolerate treatment medications because of hypersensitivity or interactions with other chronic medications; and occupational considerations).[17] The protection offered by the zoster vaccine can last three years and wanes thereafter; as such, adults receiving the vaccine before age 60 years might not be protected when their risks for herpes zoster and its complications are at their highest.[14]

Due to the recurring nature of herpes zoster infection, vaccination may be offered to suitable patients as soon as the acute stage of illness is over and the symptoms have subsided.[18] The zoster vaccine is contraindicated in persons with a history of anaphylactic reaction to gelatine, neomycin, or any other component of the vaccine, severely ill or immunosuppressed persons from any cause, whether acquired, congenital, iatrogenic or disease-based.[15] The vaccine is contraindicated in pregnancy, however it is unlikely for these women to be in the vaccine target group. Deferral of the vaccine should be considered in acute illness (e.g. in the presence of fever) or in patients with active untreated tuberculosis. While the vaccine is contraindicated in severely immunocompromised patients, it may be safely administered in people living with HIV infection with a CD4+ T cell count greater than or equal to 200 cells/mm$^3$ and who were virologically suppressed on antiretroviral therapy.[19] Zoster vaccine is not indicated for prevention of primary varicella infection (chickenpox) and should not be used in children and adolescents.[15]

While zoster vaccine is a live virus vaccine, it can be administered concurrently with all other live and inactivated vaccines, including those routinely recommended for people 60 years and older: influenza, tetanus, diphtheria and pertussis. A reduced immune response to varicella vaccine was, however, observed in persons who received concurrent administration of Pneumovax 23® and Zostavax® compared to individuals who received these vaccines four weeks apart. Due to the theoretical risk of drug interaction between the zoster vaccine and antiviral medications, persons taking chronic acyclovir, famciclovir, or valacyclovir should discontinue these medications at least 24 hours before administration of zoster vaccine, if possible. These medications should not be used for at least 14 days after vaccination, by which time the immunological effect should have been established.[17]

The live virus is not excreted in breast milk and the vaccine can therefore be administered during lactation although this will be an extremely rare consideration in the target age group for this vaccine.[15, 17]

The ACIP has recently recommended a new recombinant and adjuvant herpes zoster vaccine (Shingrix®) which has demonstrated superior efficacy when compared with Zostavax®.[20]

The most frequent reported adverse effects among vaccine recipients were mild and included e.g. reactions at the local inoculation-site and headache.[21]

## Conclusion

Shingles is an acute neurological disease that warrants immediate medical attention. Severe immune suppression as occurs with chemotherapy, chronic corticosteroid use, human immunodeficiency virus infection, some cancers, as well as old age can increase the likelihood of infection. Postherpetic neuralgia is a complication of shingles which results in pain and reduced quality of life in the affected patients. Pharmacists have a role to play in encouraging clinicians and patients on the available pharmacological and non-pharmacological treatments including referral to a pain specialist during exacerbations of PHN. It is also paramount to encourage vaccination against shingles in vulnerable patients, particularly the elderly.

## References


1. Carroll KC, Hobden JA, Miller S, et al. Jawetz, Melnick and Adelberg's Medical Microbiology. Chapter 33: Herpesviruses. Available at: http://accesspharmacy.mhmedical.com/book.aspx?bookid=1551 Accessed 30 Oct 2017.
2. Whitley RJ. Harrison's Principles of Internal Medicine: Varicella-Zoster Virus Infection. 19th edition. New York. McGraw-Hill. 2015. Available at: http://accesspharmacy.mhmedical.com Accessed 31 Oct 2017.
3. National Institute of Neurological Disorders and Stroke (NINDS). Shingles: Hope through research. Available at: https://www.ninds.nih.gov/Disorders/All-Disorders/Shingles-Information-Page Accessed 29 Oct 2017.
4. Anonymous. Epidemiology of varicella zoster virus infections. Available at: http://www.virology-online.com/viruses/VZV3.htm Accessed 30 Oct 2017.
5. Anonymous. Varicella. Available at: https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/varicella.pdf Accessed 1 Nov 2017.
6. Diplomatic, American Board of Internal Medicine, 2016: Shingles (herpes zoster). 4950 Barranca Parkway, Suite 207. California.
7. Johnson RW, Alvarez-Pasquin MJ, Bijl M, et al. 2015. Herpes zoster epidemiology, management, and disease and economic burden in Europe: a multidisciplinary perspective. Therapeutic advances in vaccines, 3(4):109-120.
8. Janniger CK. Herpes zoster. 2017. Available at https://emedicine.medscape.com/article/1132465-overview Accessed on October 2017.
9. Jung HS, Kang JK, Yoo SH. 2015. Epidemiological study on the incidence of herpes zoster in nearby Cheonan. The Korean Journal of Pain, 28(3):193-197.

10. Stankus SJ, Dlugopolski M, Packer D. Management of herpes zoster (shingles) and postherpetic neuralgia. Am Fam Physician. 2000. 15;61(8): 2437-2444 Available at: http://www.aafp.org/afp/2000/0415/p2437.html Accessed 31 Oct 2017.
11. Herrier RN, Apgar DA, Boyce RW, Foster SL. Herrier R.N., Apgar D.A., Boyce R.W., Foster S.L. Eds. Richard N. Herrier, et al.eds. Common skin disorders. Patient assessment in pharmacy. New York, NY: McGraw-Hill; 2015. Available at: http://accesspharmacy.mhmedical.com/content.aspx?bookid=1074&sectionid=62364288 Accessed October 31, 2017.
12. Janniger CK. Herpes zoster treatment and management. 2017. Available at: https://emedicine.medscape.com/article/1132465-treatment Accessed 1 Nov 2017.
13. Rossiter D, editor. South African Medicine Formulary. 12th ed, Cape Town: Health and Medical Publishing Group. 2016.
14. Gagliardi AMZ, Andriolo BNG, Torloni MR, Soares BGO. 2016. Vaccines for preventing herpes zoster in older adults. Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD008858. DOI: 10.1002/14651858.CD008858.pub3.
15. Merck Sharp & Dohme Corp. 2011. Zostavax® (varicella-zoster virus) live vaccine package insert. MSD (Pty) Ltd. Available online at http://www.merck.com/product/usa/pi_circulars/z/zostavax/zostavax_pi2.pdf Accessed 16 October, 2017.
16. Oxman MN and Levin MJ. Shingles Prevention Study Group (March 2008). Vaccination against herpes zoster and postherpetic neuralgia (PDF). The Journal of Infectious Diseases. 197 (Suppl 2): S228-36. PMC 4017882 Freely accessible. PMID 18419402. doi:10.1086/522159.
17. Centres for Disease Control and Prevention (CDC). 2011. Update on herpes zoster vaccine: licensure for persons aged 50 through 59 years. MMWR 60:1528. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a5.htm Accessed 16 October, 2017.
18. Harpaz R, Ortega-Sanchez IR, Seward JF. 2008. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 57(No. RR-5). Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm Accessed 16 October, 2017.
19. Benson CA, Hua L, Anderson JW, et al. 2012. Zostavax is generally safe and immunogenic in HIV+ adults virologically suppressed on ART: Results of a Phase 2, randomized, double-blind, placebo-controlled trial. CROI; Seattle, WA. 2012. Abstract 96.
20. Dooling K. 2017. Considerations for the use of herpes zoster vaccine. Presented at the Advisory Committee on Immunization Practices, US Centers for Disease Control and Prevention. October 25, 2017.
21. Simberkoff MS, Arbeit RD, Johnson GR, et al. 2010. Safety of herpes zoster vaccine in the shingles prevention study: a randomized trial. Ann Intern Med. 152:545-554. doi: 10.7326/0003-4819-152-9-201005040-00004.