adjusted relative risk of developing herpes zoster was 16.9 in those with HIV and the recurrence rate was 22%. Checking for HIV in at-risk populations who develop herpes zoster is recommended. While data are conflicting, there is recent evidence of a rise in cases of herpes zoster related to widespread varicella vaccination in children. This has reduced re-exposure to varicella zoster which is needed to boost waning adult T-cell-mediated immunity. The varicella vaccine for children has been government funded since late 2005 in Australia. In the subsequent three years there was a 2–3% annual increase in herpes zoster dose-specific antiviral use in adults aged 20 and over. Emergency department presentations due to herpes zoster have also increased annually by 2–6%. Similarly, general practitioner data indicate a two-fold rise in herpes zoster cases – from 1.7/1000 consultations in 2000 to 3.4/1000 in 2010. These data support the need for more widespread uptake of the licensed herpes zoster vaccine in adults. Globally there is also evidence that the rate of herpes zoster is increasing. The underlying reasons for this are probably multifactorial and include:

- the ageing of the population
- increased use of immunosuppressant drugs
- widespread childhood vaccination against varicella zoster virus.

Clinical features

Herpes zoster usually begins with a prodrome, such as pain, itching or tingling in the area that becomes affected. This may precede the characteristic rash by days or even weeks but is rarely the only clinical manifestation of varicella zoster virus reactivation (sometimes referred to as zoster sine herpete). Typically, patients experience headache, malaise and sometimes photophobia. Abnormal sensation or pain, often described as burning, throbbing or stabbing, occurs in approximately 75% of patients and may be the first noticeable feature. Often pruritus in the affected region is the most prominent feature. Allodynia, or pain induced by light touch, may also be described. Before the onset of the rash and depending on the location, symptoms may mimic pain caused by ischaemic heart disease, cholecystitis or renal colic.
Rash
The rash is usually unilateral and may affect adjacent dermatomes, with thoracic, cervical and ophthalmic involvement being the most common. Morphologically it evolves from a maculopapular rash to one comprising clusters of vesicles that ulcerate and crust over the course of 7–10 days (Fig. 1). Healing is usually complete by 2–4 weeks. When all lesions have crusted the rash is considered non-infectious. Residual scarring and pigmentation is common (Fig. 2). Once the characteristic unilateral dermatomal rash of herpes zoster appears, the differential diagnosis includes herpes simplex virus, contact dermatitis, insect bites, folliculitis, impetigo, candidiasis and scabies.

Complications
These occur in a minority of patients and are more frequent in older or immunosuppressed patients.

Postherpetic neuralgia
Postherpetic neuralgia is considered the most common complication and increases with age, affecting up to 30% of people with herpes zoster over the age of 80 years. It is generally defined as pain of at least moderate intensity persisting for three months or longer, although various definitions (and measures of pain severity) have been used in drug trials. It may occasionally last for years. Postherpetic neuralgia is characterised by constant or intermittent, usually severe, burning or lancinating pain that occurs almost daily. Alloodynia is present in most cases and can make even wearing clothing an arduous task. Quality of life is invariably reduced. Features that appear to be predictive for the development of postherpetic neuralgia include more severe initial pain, more extensive rash and age over 50 years.

Ocular involvement
Herpes zoster ophthalmicus occurs in 10–25% of cases. This involves the ophthalmic branch of the trigeminal nerve and results in a disproportionately high complication rate (50% in the absence of antiviral drugs) with the eye affected in several possible ways. Keratitis occurs in about two-thirds of cases and conjunctivitis, uveitis, retinitis and glaucoma can all occur. The presence of vesicles on the nose (Hutchinson’s sign) due to involvement of the nasociliary branch of the trigeminal nerve has been found to be highly predictive of eye involvement.

Ramsay Hunt syndrome and other neurological syndromes
Less common manifestations of zoster include the Ramsay Hunt syndrome (involvement of the geniculate ganglion of the facial nerve) which manifests as vesicles in the external auditory canal and palate associated with loss of taste to the anterior two-thirds of the tongue and facial weakness. Rarely, aseptic meningitis, myelitis, peripheral motor neuropathy, cerebellar syndromes, and stroke syndromes due to involvement of cerebral arteries (varicella zoster virus vasculopathy) can occur.

Disseminated zoster
Most individuals with herpes zoster will have some lesions outside the primary dermatome. Disseminated zoster is defined as 20 lesions or more outside the involved dermatome. It tends to occur only in immunocompromised patients and may be associated with visceral involvement (lungs, liver, gut and brain).

Bacterial infections
If bacterial superinfection is suspected, antibiotic treatment to cover Staphylococcus aureus and Streptococcus pyogenes should be considered, for
example, di/flucloxacillin 500 mg every six hours for seven days.

**Diagnosis**

The diagnosis of herpes zoster is usually clinical, with laboratory tests reserved for more atypical cases. The ideal specimen is a swab from the base of burst vesicles in viral transport medium. This can be processed for direct fluorescent antibody testing (1–2 hour turnaround time), DNA testing by PCR (turnaround time of one day, but more sensitive especially in older lesions) and viral culture (takes 1–2 weeks and is less sensitive than PCR). Serology for antibodies to varicella zoster virus usually adds little to the diagnosis and may be falsely negative in early presentation due to waning IgG antibodies below detectable levels.

**Antivirals**

Three oral nucleoside analogues – valaciclovir, famciclovir and aciclovir – are available for the treatment of herpes zoster. They reduce the severity and duration of the illness if started within 72 hours of onset of the rash. However, a Cochrane review concluded that evidence was insufficient to determine if antivirals reduce the incidence of postherpetic neuralgia, depending on the definition of postherpetic neuralgia used. All patients with zoster ophthalmicus should receive antiviral therapy even if it is delayed beyond 72 hours. Similarly, consideration should be given to treating immunocompromised patients or those with disseminated disease. Current Australian guidelines recommend famciclovir (250 mg three times a day for seven days, or if immunocompromised 500 mg three times a day for ten days) and valaciclovir (1 g three times a day for seven days) as the preferred drugs, given their greater bioavailability and less frequent dosing in comparison to aciclovir. Both the dosage and duration of antiviral treatment are greater for herpes zoster than for herpes simplex. Intravenous aciclovir (10 mg/kg three times a day) is usually reserved for immunocompromised patients with disseminated disease, severe zoster ophthalmicus or central nervous system involvement such as transverse myelitis. Dose adjustment of antivirals in addition to hydration is recommended in renal impairment to prevent nephrotoxicity and neurotoxicity. Viral resistance to the drugs is rare.

**Pain management**

Treating the pain associated with herpes zoster, particularly in the acute stage, is considered an integral component of management and may have benefits in reducing the severity and incidence of postherpetic neuralgia. This should follow a stepwise approach based on current Australian guidelines. These have been summarised in Table 1. Of note, one double-blind randomised controlled trial showed a reduction in incidence of postherpetic neuralgia at six months by about half with early (within 48 hours of rash onset) commencement of low-dose amitriptyline 25 mg at night (for 90 days) although caution must be used when treating the elderly. Pharmacological management of postherpetic neuralgia follows a similar stepwise approach and may additionally involve the use of gabapentin or pregabalin and topical capsaicin. Transcutaneous electrical nerve stimulation (TENS) may also be useful.

**When to refer for specialist assessment**

All patients with zoster ophthalmicus should be referred to an ophthalmologist to exclude eye involvement. Those with the Ramsay Hunt syndrome should be seen by an ear, nose and throat specialist. Rare neurological complications such as meningitis or myelitis usually require admission to hospital. Rapid referral to a pain clinic should be considered for patients who have a poor response to initial pain management or those with poorly responding postherpetic neuralgia.

**Vaccination**

A live attenuated herpes zoster vaccine was effective in decreasing the incidence of herpes zoster by about half and the overall burden of illness by about 60% in
Herpes zoster

people aged 60 years and over (38 546 people).4 The vaccine contained the strain used in the childhood varicella zoster virus vaccine, but was at least 14 times more potent. In the vaccine group there was a trend towards a reduction in postherpetic neuralgia cases compared with the placebo group (27/315 (8.6%) vs 80/642 (12.5%) patients). Similarly, a Cochrane review concluded that there was insufficient evidence to determine whether the vaccine was effective in preventing postherpetic neuralgia beyond its effect on reducing herpes zoster.5

A large US retrospective cohort study reviewed 75 761 vaccine recipients and found a 55% reduction in herpes zoster (across all age groups) in addition to a 63% reduction in zoster ophthalmicus and a 65% reduction in hospital admissions. More recently, a multicentre study involving 22 439 patients in the 50–59 years age group showed a 70% reduction in herpes zoster.6

The zoster virus vaccine has been recommended by the US Advisory Committee for Immunization Practices since 2006 and in Australia7 since 2009 for those aged 60 years or older. In March 2011 the Food and Drug Administration approved its use in the US in those aged 50–59 years.7 It can be given to people who have had previous episodes of zoster (although at least one year after the last episode of zoster has been suggested) or in those with underlying chronic conditions. However, it is currently contraindicated in people with significant immune impairment, for example those on high-dose steroids, or patients referred to a pain specialist promptly.

Antivirals are effective in limiting herpes zoster if given within 72 hours of the rash appearing. Pain associated with herpes zoster should be treated early and if a patient responds poorly, they should be referred to a pain specialist promptly.

The zoster vaccine is the best way to prevent herpes zoster and its associated complications such as postherpetic neuralgia.8

**Preventing transmission**

Transmission of varicella zoster virus from a patient with herpes zoster to susceptible contacts is thought to be much lower than with chickenpox although recent evidence of detection of virus in the saliva of a majority of patients with herpes zoster points to a possibly greater risk than previously thought.9 Preventing such transmission via direct contact and aerosolisation can be done by covering non-crusted lesions with a light non-adherent padding dressing10 after bathing regularly with saline to remove exudate and crusts. Patients should be instructed to avoid susceptible contacts especially those who are pregnant or immunocompromised.

**Conclusion**

A booster is not currently recommended. Serological testing to elicit varicella zoster virus immune status before or after the vaccine is not necessary. It is not useful for the treatment of acute herpes zoster.14

The herpes zoster vaccine should be routinely offered to those 60 years or older and can be considered in those aged 50–59 years. Unfortunately, vaccine availability has been limited in Australia. Reliable supplies are expected in 2013. The vaccine is not currently subsidised.

**REFERENCES**


**SELF-TEST QUESTIONS**

**True or false?**

1. Famiclovir reduces the severity and duration of herpes zoster if started 4 days after the appearance of a rash.

2. The zoster virus vaccine reduces disease in people aged 60 and over.

**Answers on page 171**

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**Book review**

*Australian Don't rush to crush handbook*. 1st edition.

Society of Hospital Pharmacists of Australia
Collingwood, Vic: SHPA; 2011.
647 pages
Price: $120 ($110 for members of the SHPA)

This is the first edition of 'Don't rush to crush', by the Society of Hospital Pharmacists of Australia. It is focused on providing a comprehensive selection of Australian-based medication monographs to guide healthcare professionals in the safe administration of medications to people unable to swallow solid oral medicines. It is not designed to replace the approved product information, it is a companion to the clinical decision-making process.

The handbook introduction provides a comprehensive outline of the problems and implications of medication-swallowing difficulties and the alteration of solid oral medications for both general patients and those having enteral feeding. There is a description of the common methods used to alter medications, medications that shouldn’t be crushed and a section focusing on the specifics of administering medicines to people with swallowing difficulties or enteral feeding tubes. This section is particularly useful clinically as it contains decision trees and administration flow charts to assist with the practicalities of altering and administering the medications, including preparation details for dispersible tablets, crushed tablets and dispersible capsules.

A great strength of the monographs themselves is their simplicity. Aside from the usual details including generic and brand names, strength and dosage form, a symbol-based quick guide allows the user to easily identify whether a product can be dispersed, crushed, not crushed, is hazardous or cytotoxic, or if it is available as a liquid formulation. For each monograph, specific advice is given for both enteral feeding and general swallowing difficulties.

This handbook would be a valuable resource in all clinical settings including hospital, rehabilitation services, aged care, domiciliary care and general practice.

It is practical and comprehensive, and its Australian-based monographs make it the most worthwhile reference source of this kind available and a ‘must have’ for anyone working with medications.