

Shingles vaccine

Is it worth the effort?

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Studies in more than 150,000 people suggest the shingles (zoster) vaccine can halve the incidence of herpes zoster and reduce its complications even more in people aged 60 years and over.

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CASE SCENARIO

Jessie, aged 72 years, has just returned from a holiday in the USA. During the trip she met several Americans around her age who had been given 'shingles vaccine' by their local doctors. They were surprised that Jessie had never heard of shingles vaccine and even more surprised that it was not promoted strongly in Australia for those aged over 65 years.

Jessie comes to see you to ask about the vaccine and whether she should have it. She is in good health with treated stable hypertension and takes statins for hypercholesterolaemia. She says she had a severe bout of chickenpox when she was in primary school.

COMMENTARY

It is true that there has been little publicity about the shingles (zoster) vaccine in Australia since it was recommended in 2009 in the *Australian Immunisation Handbook* for all adults aged 60 years or older.¹ The main reasons are probably the relative scarcity of this vaccine in Australia until recently and the



Figure. Shingles involving the eye (herpes zoster ophthalmicus). Direct eye involvement is a common complication of herpes zoster affecting the ophthalmic branch of the trigeminal nerve.

vaccine's cost. The adult varicella zoster vaccine is 14 times more potent than the monovalent childhood varicella zoster vaccine and therefore requires significantly more live attenuated virus to manufacture. It costs around \$180 to \$200, excluding the cost of administration.

In the USA, the zoster vaccine has been approved since 2006 for those aged 60 years and over, and since 2011 for those aged 50 years and over. Since 2008, the US Centers for Disease Control and Prevention (CDC) have recommended routine use of the vaccine in all persons aged 60 years and over unless it is contraindicated.

In Australia, the TGA has approved the zoster vaccine for prevention of herpes zoster (shingles) in people aged 50 years and over as well as for prevention of postherpetic neuralgia (PHN) and reduction of acute and chronic zoster-associated pain in those aged 60 years and over. The vaccine is in the early stages of assessment for PBS listing.

Risk of herpes zoster

In Jessie's case, her history of chickenpox as a child certainly puts her at risk of herpes zoster, along with about 90% of the population who have likewise been exposed to chickenpox. About a third of these people will experience herpes zoster during their lifetime, with the incidence greatest after the age of 60 years. Furthermore, it is now recognised that recurrent episodes of herpes zoster are more common than previously thought, with the chance of recurrence over an eight-year period being 4% for men, 7% for women and approximately 20% for people with HIV infection.

General practitioner data in Australia suggest that the number of cases of herpes zoster doubled between 2000 and 2010.² The reasons are thought to be a combination of the ageing of the population and the increased use of immunosuppressant medications. It is also possible that the widespread use of varicella vaccine for children and nonimmune adults (introduced in Australia in

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2005) may have reduced the opportunities for re-exposure to varicella zoster virus in the community; re-exposure may boost waning immunity in adults.

Risk of complications

Should Jessie develop herpes zoster, she is at risk of developing PHN, which is considered to be more severe in patients older than 70 years. PHN is generally defined as moderately severe pain in the distribution of the shingles attack that persists for at least three months and may be associated with a reduction in quality of life. In up to 50% of patients with PHN, pain is not effectively relieved despite treatment, and occasionally it persists for years.

Features that are predictive for the development of PHN include more severe initial pain, more extensive rash and age over 50 years. In people over the age of 80 years, PHN is estimated to occur in about 30% of people with herpes zoster.

Should Jessie have the added misfortune of a herpes zoster attack involving the ophthalmic branch of the trigeminal nerve (herpes zoster ophthalmicus), she has a significant chance of direct eye involvement (about 50% in the absence of antivirals; Figure). Neurological complications such as meningitis, myelopathy and cerebellitis also occur less commonly.

Vaccination prevents shingles and postherpetic neuralgia

Early research found that the childhood varicella vaccine was not effective in boosting cell-mediated immunity to varicella zoster virus in older people. Much higher levels of attenuated virus were required to elicit and maintain immunity, probably as a consequence of decreased responsiveness to vaccines in older people in general.³

Since 2005, several large studies have been published demonstrating efficacy of the adult zoster vaccine. The Shingles Prevention Study, involving 38,546 patients aged 60 years and over, showed a 50% overall reduction in shingles cases (64% for those from 60 to 69 years and 41% for those from 70 to 79 years).⁴ There was also a 67% reduction in PHN in those aged 60 years or older. The primary study endpoint, however, was burden of illness due to herpes zoster. This was measured by a severity of illness score defined by the area under the curve of herpes zoster pain (based on responses to the 'worst pain' question in the Zoster Brief Pain Inventory) plotted against time in the six months after rash onset. This burden of illness score was reduced by 61% in those who received the vaccine (66% in the 60 to 69 years age group and 55% in the 70 years and over age group). Furthermore, the number of severe cases of PHN (more than 80 days of the 'worst pain imaginable') was reduced by 82%, and 80% of these cases occurred in those aged 70 years or over.⁵

A further large study of 75,761 people who received the zoster vaccine found a 55% reduction in herpes zoster (across all age groups) in addition to around a 60% reduction in zoster ophthalmicus and in hospital admissions when compared with unvaccinated age-matched controls.⁶ Another study reviewing the vaccine in over 22,000 people aged from 50 to 59 years found

the vaccine well tolerated, with an efficacy of 70%.⁷

Most recently, a much larger American cohort study involving 766,330 randomly selected people aged 65 years or over found vaccine efficacy of 48% (37% if immunocompromised) in almost 30,000 herpes zoster vaccine recipients (more than 4000 of whom were considered immunocompromised).⁸ A 59% reduction in PHN was also found in this study.

Tolerability and administration of zoster vaccine

Although injection site reactions occur in up to a third of patients who receive zoster vaccine, these are generally mild. There is no difference in serious adverse events when zoster vaccine is compared with placebo. The vaccine can be given to patients who have already had herpes zoster, although it is suggested that they wait at least a year after the attack. Although zoster vaccine can be given concurrently with influenza vaccine, it should not be given within one month of pneumococcal vaccine.

Booster doses of zoster vaccine are not currently recommended. Zoster vaccine is contraindicated in people with significant immune impairment, such as those taking high-dose corticosteroids and those with HIV infection who have a CD4+ T-cell count less than 200 cells/ μ L.

CONCLUSION

Jessie is likely to benefit from zoster vaccine. If she is willing to be vaccinated and the vaccine cost is not an issue then we believe it should be offered. At her age, zoster vaccination reduces the risk of herpes zoster by about half and is expected to reduce the risk of complications such as PHN or zoster ophthalmicus to an even greater extent.

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