SIGMA CANADIAN MENOPAUSE SOCIETY

HERPES ZOSTER VACCINATION:
Frequently Asked Questions

CANADIAN MENOPAUSE SOCIETY

SOCIÉTÉ CANADIENNE DE MÉNOPAUSE

Preface

Thanks to Dr. Marla Shapiro and colleagues, "Herpes Zoster Vaccination: FAQs" was first published in 2012. It was so popular that we had to do a second reprint the following year.

With newer research results and data, minor changes were made to this 2nd edition to keep the brochure current.

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A family practitioner's guide.

Herpes zoster (HZ), or shingles, results from reactivation of the varicella-zoster virus (VZV), which lies dormant in the spinal and cranial sensory ganglia following a primary infection with varicella (chickenpox), usually during childhood. Herpes zoster is characterized by a unilateral, cutaneous, usually painful vesicular rash that typically presents in a single dermatome. Complications of HZ can include sight-threatening infections, central nervous system infections, nerve palsies, neuromuscular disease (including Guillain-Barré syndrome), and secondary bacterial infections, to name a few.[1] However, postherpetic neuralgia (PHN) is its most common and serious complication. In Canada there are 130,000 cases of HZ and 17,000 cases of associated PHN each year.[2]

Neuralgic pain might develop before the HZ rash; in some cases, the classic HZ rash might not even appear (zoster sine herpete). PHN is characterized by prolonged and often debilitating neurogenic pain that persists for more than 90 days from rash onset. The incidence is directly related to age.[3] This complication occurs in approximately 20% of adults with HZ and in one-third or more of octogenarians and often has a major adverse impact on quality of life, especially in elderly persons.[4] Half of patients who continue to suffer after 1 year will continue to have unrelieved pain, which will inevitably affect quality of life.[5]

Postherpetic neuralgia is notoriously difficult and sometimes even impossible to treat, despite the use of strong analgesics such as opioids. Pathologic evidence suggests that VZV can cause permanent peripheral and central nervous system damage,[5] destroying sites of intrinsic pain inhibitory mechanisms where analgesics act; as a result, patients are left inadequately relieved by, or refractory to, all drugs for pain. Antiviral medications, even when initiated within 72 hours

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of onset, are only marginally effective for the prevention of PHN.[6] The vaccine reduces the incidence of HZ by about 50% and the occurrence of PHN by two-thirds, with vaccinated individuals experiencing attenuated or shortened symptoms. The vaccine has few adverse effects, primarily injection site reactions.[9] It is now approved in Canada for immunocompetent adults aged 50 years of age and older.[1,10]

KEY POINTS

The greatest benefit of the herpes zoster (HZ) vaccine is its prevention of postherpetic neuralgia, which can be extremely difficult to treat. Clinical trials have demonstrated the efficacy of the vaccine. This live virus vaccine is contraindicated in many immunocompromised individuals. The Canadian National Advisory Committee on Immunization (NACI) states that the vaccine may be administered to individuals on low dose immunosuppressive therapy and to individuals on anti-TNF biologics on a case by case basis after review with an expert in immunodeficiency. Those taking antiviral medications against the HZ virus should cease treatment at least 24 hours before administration of the vaccine and avoid restarting treatment for at least 2 weeks after. Side effects typically involve injection site reactions (e.g., erythema, pain, pruritus). However, the burden of HZ and postherpetic neuralgia is such that NACI recommends routine vaccination in adults 60 years of age and older without contraindications and individuals 50 to 59 years old can be considered for immunization. ZOSTAVAX®II is refrigerator-stable. Many health insurance companies reimburse the vaccine.[4]

HERPES ZOSTER VACCINATION: FAQ

The following questions are routinely posed by practitioners regarding the use of the HZ vaccine; the answers can serve as a useful guide in family practice.

WHAT IS THE DURATION OF PROTECTION PROVIDED BY THE VACCINE?

The duration of protection is not currently known. In the Shingles Prevention Study (SPS), vaccine efficacy was maintained through 4 years of follow-up.[7,8] In the Short-Term Persistence Study (STPS) the vaccine efficacy was maintained through 5 years of follow up (Schmader 2012). The long-term persistence study (LTPS) demonstrated further vaccine efficacy for up to 11 years post-vaccination. There was a decline in vaccine efficacy but protection remained significantly greater than zero through 8-10 years. (Morrison 2015)

WHAT IS THE EFFICACY OF THIS VACCINE?

The pivotal efficacy trial for the HZ vaccine (i.e., the SPS) included more than 38,500 adults 60 years of age and older. In that study, the vaccine reduced the incidence of shingles by 51% and the incidence of persistent, severe pain after shingles (i.e., PHN) by 66.5%.[7]

CAN THE VACCINE BE GIVEN TO ADULTS AGED 50 TO 59 YEARS?

Yes. In May 2011 Health Canada extended the indication of the HZ vaccine to those 50 years and older based on data from a large randomized, double-blind, placebo-controlled trial of people between 50 and 59 years of age (N = 22,439). The study demonstrated that the vaccine was safe and reduced the incidence of HZ (2.0 cases per 1,000 person-years vs. 6.6 cases per 1,000 person-years in the placebo group), with a protective efficacy against HZ of 69.8%.[8,13] Further, NACI also recommends that the HZ vaccine can be considered in patients 50 years of age and older.[1]

ARE CERTAIN POPULATIONS AT INCREASED RISK FOR HERPES ZOSTER?

Studies show that patients with co-morbid diseases such as diabetes[9], COPD[10] and family history[11] are at increased risk for developing herpes zoster.

WILL THE VACCINE BENEFIT PATIENTS WHO HAVE ALREADY HAD HZ?

Having an episode of HZ has an immunizing effect, greatly reducing the probability of a second event.[14] Patients with a history of severe HZ are often the most insistent on receiving the vaccine,[15] and concerns have been raised about the validity of patient histories of HZ. HZ vaccine may be administered to individuals > 50 years old with a prior history of HZ. Based on expert opinion, it is recommended that the vaccine be given at least 1 year following the last episode of herpes zoster. (NACI 2014)

CAN THE HZ VACCINE BE ADMINISTERED TO THOSE WITH AN UNKNOWN HISTORY OF CHICKENPOX?

Yes. An estimated 90% of Canadian adults have had a previous VZV infection. Thus, almost all adults 60 years of age or older have been infected with VZV, regardless of patient reported history or recall. There is no need to test immunity levels before administering the vaccine. However, if a patient is known to be susceptible to VZV, it is recommended that 2 doses of the varicella vaccine be administered, at least 4 weeks apart, rather than administering the HZ vaccine.[12,16,17]

CAN THE VACCINE BE GIVEN CONCURRENTLY WITH OTHER VACCINES?

The HZ vaccine is a live, attenuated virus vaccine. Influenza vaccine (NACI 2010) and pneumococcal vaccine (NACI 2014) may be administered concomitantly with HZ vaccine at a different body injection site.

WHAT CONSTITUTES IMMUNOCOMPROMISED FOR VACCINE CONTRAINDICATION?

The ACIP states that people with primary or acquired immunodeficiency should not receive the vaccine. Those anticipating initiation of immunosuppressive therapy, or who have diseases that might lead to immunodeficiency, should receive 1 dose of HZ vaccine at least 14 days before beginning immunosuppressive therapy.[9] More detail is available in Table 1.[12,18]

There remains a large "gray area" for mildly to moderately immunocompromised patients in whom the risk-benefit ratio of vaccination is not well understood. The potential risks of vaccinating patients receiving immunosuppressive drug therapies (e.g., methotrexate or tumour necrosis factor-α inhibitors) or with illnesses that alter the immune system (e.g., systemic lupus erythematosus or low-grade chronic lymphocytic leukemia) remain unknown. However, extreme old age (80 years of age and older) and the presence of medical comorbidities, such as diabetes mellitus, coronary artery disease, or hypertension, are not contraindications to vaccination.[14]

*See Page 9 for Table 1

TABLE 1. POSSIBLE CONTRAINDICATIONS FOR HERPES ZOSTER VACCINATION IN IMMUNOCOMPROMISED PATIENTS

REASON FOR IMMUNODEFICIENCY	CAN THE VACCINE BE CONSIDERED?
Bone marrow or lymphatic cancers (including leukemias and lymphomas)	No
Leukemia in remission and no radiotherapy or chemotherapy for at least 3 months	Yes
AIDS or manifestations of HIV (including CD4-positive T lymphocyte counts of less than 200/mm^3 or less than 15% of the total lymphocyte count)	No
Prednisone (or an equivalent corticosteroid): 20 mg/d or more for 2 weeks	No
Prednisone (or equivalent corticosteroid): less than 20 mg/d and not as chronic daily therapy*	Yes
Topical, intranasal, inhaled, and intra-articular corticosteroid use	Yes
Bursal or tendon corticosteroid injections	Yes
Methotrexate: less than 0.4 mg/kg weekly	Yes
Azathioprine: more than 3 mg/kg daily	No
Mercaptopurine: more than 1.5 mg/kg weekly	No
Evidence (laboratory or clinical) of cellular immune deficiency	No
Impaired humoural immunity (e.g., dysgammaglobulinemia, hypogammaglobulinemia)	Yes
Planned hematopoietic stem cell transplantation	Limited evidence–assess patient-relevant risk
2 or more years post–hematopoietic stem cell transplantation	Yes
Recombinant human immune mediators and immune modulators, particularly tumour necrosis factor inhibitors; the ACIP recommends deferring vaccination for at least 1 month after discontinuation of these therapies	No

ACIP-Advisory Committee on Immunization Practices, CD-cluster of differentiation.
* Recent results from a clinical trial indicate the zoster vaccine was well tolerated in subjects administered daily doses of 5-20 mg prednisone.[19]

CAN AN ADULT RECEIVE THE VACCINE IF THERE IS AN IMMUNOCOMPROMISED VZV-SERONEGATIVE INDIVIDUAL RESIDING IN THE SAME HOUSEHOLD?

Yes. Person-to-person transmission of the vaccine virus was not reported in HZ vaccine clinical trials. Postmarketing experience with varicella vaccine suggests that transmission (although rare) might occur between susceptible contacts and vaccinated individuals who develop a varicella-like rash.[8,12] After HZ vaccination, precautions are needed only if a varicella-like rash develops in individuals who are in close contact with people at risk of severe varicella.[12]

CAN THE VACCINE CAUSE THE DISEASE?

The likelihood of vaccination causing a case of HZ appears to be very low. In clinical trials with Zostavax the vaccine strain of the virus was not detected in any of the postvaccination HZ-like rashes that were available for polymerase chain reaction testing.[7,8,22]

CAN THE VACCINE BE ADMINISTERED TO PATIENTS TAKING ANTIVIRAL MEDICATION?

Antivirals active against HZ (acyclovir, famciclovir, and valacyclovir) might interfere with replication of the live VZV-based vaccine. Consequently, patients taking antiviral medications active against HZ should discontinue these medications for at least 24 hours before the administration of the vaccine,[20] and should not restart them for at least 14 days after vaccination. Current NACI recommendations suggest that individuals taking antivirals at the time of vaccination might benefit from a second dose of vaccine at least 42 days after the first dose and after discontinuation of antiviral therapy.[1]

WHAT HAPPENS IF THE VACCINE IS GIVEN INTRAMUSCULARLY INSTEAD OF SUBCUTANEOUSLY?

Although the vaccine is meant to be administered subcutaneously, it is not necessary to repeat immunization if it is given intramuscularly.[8]

WHAT ABOUT PATIENTS WHO TAKE ACETYLSALICYLIC ACID (ASA) ON A DAILY BASIS—CAN THEY TAKE THIS VACCINE?

Guidelines for the chickenpox (varicella) vaccine for children—which is different from the vaccine for adults—state that ASA should not be used to treat fever related to vaccinations in children because of the rare, but possible, association with Reye syndrome. This association does not exist with adults. Therefore, adults receiving long-term ASA therapy should be vaccinated if indicated.[21]

SHOULD THE HZ VACCINE BE GIVEN TO PEOPLE WHO HAVE BEEN IMMUNIZED WITH A VARICELLA VIRUS VACCINE?

No. People who have immunity to chickenpox through vaccination do not appear to be at risk of severe HZ, and it is not recommended that they be vaccinated against shingles.[11] That said, health care providers do not need to inquire about previous VZV vaccination before administering the HZ vaccine, as so few people in the age group for which HZ vaccination is recommended have had VZV vaccination.[12]

HOW SHOULD THE VACCINE BE STORED?

ZOSTAVAX®II should be stored refrigerated at a temperature of 2 to 8°C or colder until reconstituted for injection. The diluent should be stored separately at room temperature (20-25°C) or in the refrigerator (2 to 8°C). The vaccine should be administered within 30 minutes after reconstitution in order to minimize loss of potency.

WHAT SIDE EFFECTS SHOULD PHYSICIANS BE CONCERNED ABOUT?

Overall, the HZ vaccine has a low incidence of side effects. The safety of the vaccine has been studied in more than 20,000 adults 50 years of age or older in clinical trials. In the SPS, injection site reactions (erythema, pain, swelling, pruritus, warmth, and hematoma) occurred in 48% of people who received the vaccine (versus 17% in the placebo arm).[8] Further details are provided in Table 2.[8,22] and also from a large managed-care cohort study: a Vaccine Safety Datalink study, from Tseng et al. J of Internal Med 2012 reported safety data for more than 193,000 vaccinated individuals.

TABLE 2.

VACCINE-RELATED INJECTION-SITE AND SYSTEMIC ADVERSE EXPERIENCES REPORTED IN 1% OF ADULTS WHO RECEIVED ZOSTAVAX® OR PLACEBO 1-42 DAYS POSTVACCINATION IN THE ZOSTAVAX® EFFICACY AND SAFETY TRIAL

Adverse Experience	Zostavax (N=11,904) %	Placebo (N=11,116) %
Injection site reactions:		
• Pain	53.9	9.0
• Erythema	48.1	4.3
• Swelling	40.4	2.8
• Pruritus	11.3	0.7
• Warmth	3.7	0.2
• Hematoma	1.6	1.6
• Induration	1.1	0.0
Systemic:		
• Headache	9.4	8.2
• Pain in extremity	1.3	0.8

HOW MANY PEOPLE NEED TO BE VACCINATED TO PREVENT 1 CASE OF HZ OR PHN?

To prevent 1 case of HZ and 1 case of PHN in individuals 65 years of age and older, 11 and 43 people, respectively, need to be vaccinated.[23]

WILL THE VARICELLA IMMUNIZATION PROGRAM AFFECT THE INCIDENCE OF SHINGLES?

Some studies suggest that immunity to VZV is boosted through repeated exposure to varicella or HZ in adulthood. While it is plausible that a sufficient number of varicella exposures can reduce the risk of HZ in select populations, it remains unclear whether such levels of exposure have an epidemiologically important role in reducing the risk of HZ among the general population of older adults.[12,24,25]

SHOULD THE VACCINE BE USED IN PEOPLE OLDER THAN THE AGE OF 80?

Those older than 80 years are at the greatest risk for HZ and PHN. A recent large retrospective cohort study for Zostavax demonstrated that vaccine effectiveness was maintained across all age strata, including the oldest vaccine recipients (P = .62).[26] The safety of herpes zoster vaccine has been demonstrated in patients 80-89 years old (n=3039) and 90+ (n=169) (Baxter 2012).

Neither Health Canada nor NACI have set an upper age limit on the use of the vaccine,[1] while the ACIP recommends that the vaccine be offered to all eligible people, including older individuals, frail individuals, and individuals with chronic illnesses.[27] Heterogeneity of health makes age criteria much less helpful. A "non-frail" 85-year-old might derive similar or enhanced benefit from the vaccine compared with a "frail" 75-year-old.

CONCLUSION

The HZ vaccine is safe and effective in reducing the incidence of HZ and PHN, as well as in attenuating the severity of HZ disease in older adults. The NACI advises that the vaccine be recommended for all adults aged 60 years and older and be considered in those older than 50 years.[1]

In Canada, direct medical costs are approximately $68 million annually for the diagnosis and treatment of HZ and its complications.[2] However, results of economic studies suggest that vaccinating adults with the HZ vaccine, especially individuals aged 60 to 75 years, is a cost-effective intervention and a judicious use of scarce health care resources, particularly in light of the large aging population.[28,29]

The data support HZ vaccination as a feasible and safe prevention strategy for reducing the overall burden of HZ. Herpes zoster vaccination should become an integral part of the promotion of healthy aging.

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COMPETING INTERESTS

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