

2 Dose Varicella Immunization Program in BC
Information for Healthcare Providers
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Archived

1. What were the varicella and MMR immunization program changes as of January 1, 2012? What is the current program change?

Varicella

- A 2nd dose of varicella vaccine is routinely offered at school entry (4-6 years of age).

MMR

- A 2nd dose of MMR vaccine is routinely offered at school entry instead of 18 months of age.
- A combined MMRV vaccine will be used in the BC program starting about January 2015. The MMRV combination vaccine will replace the use of separate injection 2nd doses of MMR and varicella at school entry.

Starting in the 2012/2013 school year:

- A 2nd dose of varicella vaccine will be routinely offered to those in grade 6.

2. What is the rationale for moving to a 2 dose varicella immunization schedule?

The National Advisory Committee on Immunization (NACI) reports that 2 doses of varicella vaccine have been projected to decrease varicella cases by an additional 22% when compared to 1 dose only.¹ Both primary and secondary vaccine failure contribute to “breakthrough” varicella disease (also called “vaccine modified”) in immunized persons following the 1st dose of varicella vaccine.

Primary vaccine failure or failure to mount a protective immune response following vaccination occurs in 3-24% of persons depending on the type of antibody measured. Secondary vaccine failure, or waning immunity, is also thought to occur following varicella vaccination and is due to loss of some protection over time.

In one US study indicative of waning immunity, the annual rates of breakthrough varicella disease were:²

- 1.6 cases/1000 persons at 1 year after vaccination
- 9 cases/1000 persons at 5 years after vaccination
- 58.2 cases/1000 persons at 9 years after vaccination

A third reason for lack of varicella immunity is lack of vaccination. An estimated 20% or more of grade 6 students may not have been immunized at school entry based on uptake data from the first years of the varicella vaccine school entry program in BC. However, some of these children may have naturally acquired immunity due to wild type infection.

3. Who is NOT eligible for 2 doses of varicella vaccine?

Those who need not or should not be immunized include those with:

- A self reported history of wild type varicella disease at ≥ 12 months of age
- A history of physician diagnosed herpes zoster (shingles) ≥ 12 months of age
- A contraindication to varicella vaccination
- Laboratory confirmed varicella disease or laboratory confirmed immunity to varicella
- Those who are ≥ 13 years of age and who have a history of prior varicella vaccination with 1 dose when < 13 years of age may benefit from a 2nd dose of varicella vaccine, but are not eligible to receive publicly funded varicella vaccine at this time.

4. What do we say to the parents who want their adolescent (≥ 13 years of age) to have a 2nd dose of varicella vaccine?

There is currently no recommendation from NACI regarding adolescents who have received 1 dose of varicella vaccine < 13 years. A 2nd dose may be of benefit for older children who have received 1 dose of vaccine in the past; however, it is not currently publicly funded. Parents of these children may wish to purchase a 2nd dose. The age of eligibility for the 2nd dose varicella will change over time. See answer to Question 7.

5. Why are all immunizations not publicly funded?

Decisions to fund vaccine programs are made by the Ministry of Health based on recommendations by the Communicable Disease Policy Advisory Committee chaired by the Provincial Health Officer. This expert committee makes recommendations based on epidemiology, the best available scientific evidence, and the advice of national and international expert groups, which are then prioritized against other public health initiatives.

6. Who is considered up-to-date for age within the 2 dose varicella immunization program?

Up-to-date for age is a concept used to assess a person's immunization record against the BC immunization program schedule.

As of January 1 2012:

- Children ≥ 12 months and < 4 years of age with 1 dose of the vaccine
- Children ≥ 4 and < 7 years of age with 2 doses of the vaccine received ≥ 3 months apart

Because the introduction of the 2nd dose at school entry in BC was implemented for children in conjunction with the school-entry DaPT–IPV vaccine, children in this 3-year age group who received their school entry dose prior to January 2012 may not have received a 2nd dose of varicella vaccine.

These may be immunized opportunistically in future years, or routinely offered the 2nd varicella dose when in grade 6.

Starting in the 2012/13 school year:

- Children ≥ 7 years of age but before completion of grade 6 who have received 1 dose of varicella vaccine given at ≥ 12 months of age are considered up-to-date for age until grade 6
- Children who have completed grade 6 on or after June 30, 2013 will be considered up-to-date for age if they have received 2 doses of varicella vaccine ≥ 3 months apart with the first dose given at ≥ 12 months of age

Adolescents:

Those who completed grade 6 as of June 30, 2012 who have received 1 dose of varicella vaccine given at ≥ 12 months of age are considered up-to-date for age in the BC program. See answer to Question 4.

7. Does the “once eligible, always eligible” principle apply to the 2 dose varicella immunization program?

The “once eligible, always eligible” principle applies to the 2 dose varicella immunization program as outlined below. In BC, routine varicella vaccination was introduced as shown in this table:

Varilrix®	2004	• Susceptible children at school entry and Grade 6 (birth year cohorts 1993 and 1999)
Varivax® III	2005 (January)	• Susceptible infants at ≥ 12 months of age (infants born on or after January 1, 2004)

Children who were eligible for their 1st dose of varicella vaccine at ≥ 12 months of age or at school entry are eligible to receive a 2nd dose. This is effective for

those born in 1999 and later. The majority of this cohort will have received vaccine derived immunity rather than being naturally infected. In contrast, the majority of those immunized in the early years of the varicella program in grade 6 would have wild type immunity.

8. Why are we not using MMRV vaccine at 12 months of age?

The BC Communicable Disease Policy Advisory Committee reviewed the option of using MMRV at 12 months of age. This committee concluded that separate MMR and varicella vaccines are preferable because MMRV is associated with an excess risk of febrile seizures of about 1/ 2200 recipients in this age group.³ This risk is not seen at older ages such as school entry.

9. How will we use the combined MMRV vaccine when children have already received either a 2nd dose of MMR or varicella vaccine?

The combined MMRV vaccine will not be used in BC until about January 2015. At that time, MMRV vaccine will be routinely offered at school entry (4-6 years of age). MMR and varicella vaccines will continue to be available in BC and children who do not require a 2nd dose of both at school entry may be immunized with the vaccine they require.

As of January 1 2012, children who have already received a 2nd dose of MMR at 18 months will only be offered varicella vaccine at school entry. Children older than infancy moving to BC who have not received their 1st dose of either MMR or varicella vaccine should be offered MMR and varicella by separate injection, at their first immunization visit.

10. Children will now be receiving a 2nd dose of MMR vaccine at school entry instead of at 18 months. Does this leave them at risk for measles, mumps, or rubella?

While there is a small window of susceptibility to measles and mumps by delaying the 2nd dose to school entry, this is very unlikely to result in infection. The NACI schedule for the 2nd dose of MMR is permissive for administration at either 18 months or 4-6 years; Alberta, Manitoba, Nova Scotia and Ontario administer the 2nd dose of MMR at school entry.⁴ Based on measles reporting since the 2nd dose of MMR was added to the schedule in 1996 in Canada, the above provinces have achieved measles control comparable to that in BC without higher rates observed in children between the ages of 1 and 5 years. Mumps is uncommon in BC and occurs more with waning immunity and exposures associated with young adulthood; young children rarely get mumps and rates of mumps are not higher in preschoolers in provinces with a 2nd dose of

MMR at school entry. Achieving and maintaining high immunization rates is the key factor related to population level protection.

11. What is the rationale for offering the 2nd dose of varicella vaccine at school entry instead of at 18 months?

The expert opinions of NACI and the U.S. based Advisory Committee on Immunization Practices (ACIP) are supportive of providing a 2nd dose of varicella vaccine before the 13th birthday to boost waning immunity.^{1,9} Giving the 2nd dose later in childhood may provide better immunity lasting into young adulthood and this will counter waning immunity.

A 2nd dose varicella program at preadolescence was found to be the most cost effective strategy in a Canadian analysis (Brisson M., unpublished). Further, in BC, school entry is currently the least 'crowded' milestone with respect to other vaccines given and a 2nd varicella dose added to the schedule at this age was deemed most operationally feasible by the BC Immunization Committee (BCIC).

12. What is the expected follow-up of children who were not offered a 2nd dose of varicella vaccine at school entry?

As of January 1 2012, children who were not offered a 2nd dose of varicella vaccine at school entry and who have not yet entered grade 6 can be offered the varicella vaccine on an opportunistic basis. Starting with the 2012/2013 school year, the grade 6 immunization program will be an opportunity to provide a 2nd dose of varicella vaccine.

13. How long will a 2nd dose of varicella vaccine be offered to grade 6 students?

The grade 6 varicella immunization program will run until approximately 2016/2017. By this time, most grade 6 students would have received a 2nd dose of varicella vaccine at school entry. Thereafter, grade 6 will remain an opportunity to update childhood immunizations as needed.

14. Are there studies showing the effectiveness of providing the 2nd dose of varicella vaccine at school entry or in grade 6?

There are no data available from clinical trials that have specifically examined the question of vaccine effectiveness using different ages for receipt of the 2nd dose. There are data from studies in children who received the 2nd dose at ages up to 12 years old that indicate higher protection against varicella disease in such 2 dose recipients.⁵

15. What are the recommended intervals between 2 doses of varicella vaccine?

Varicella vaccine name	Children ≥ 12 months to < 13 years of age	Persons ≥ 13 years of age
Varilrix®*	≥ 3 months between doses 1 and 2	≥ 6 weeks between doses 1 and 2
Varivax® III		

*At the time of writing, the varicella immunization product being used in BC is Varilrix®.

16. What is the rationale for the different age specific minimum intervals for varicella vaccines?

The minimum intervals for the 2 dose varicella vaccine series are based on clinical trials and expert opinion as cited by NACI.¹ The ideal timing of the 2nd dose of varicella vaccine has not been systematically studied.

17. Historically the varicella vaccine minimum interval was 4 weeks. Are doses given in the past using the 4 week minimum interval valid?

Historically, 2 doses of the varicella vaccine were only given to those ≥ 13 years of age. Therefore, 2 doses of varicella vaccine given in the past using the 4 week minimum interval are valid, but should have only been given to those ≥ 13 years of age. NACI outlines the recommended intervals for varicella vaccine series based on the client's age and the product being used.¹

For children < 13 years of age, the recommended interval between 2 doses of varicella vaccine is 3 months regardless of which products are used. Children should be scheduled for vaccination based on the recommended intervals. The Varilrix® product monograph states that 6 weeks is the minimum interval between doses in children <13 years of age. However, if a 2nd dose was given at least 4 weeks after the first, a 3rd dose should not be administered and the 2nd dose should be considered valid.⁶

18. What if a child presents for a 2nd dose of varicella vaccine and the 1st dose product type is unknown?

Any varicella vaccine may be used to complete the series. For programmatic reasons, the use of a different product for the 2nd dose of varicella vaccine may be necessary because any given jurisdiction may carry only one type of varicella vaccine during a contract period. According to NACI there are no published data on the interchangeability of the 2 available univalent varicella vaccines (Varivax® III and Varilrix®) in a 2 dose primary schedule.¹ However there is no biological

reason to assume a difference in response because both vaccines contain the Oka-strain of live attenuated varicella virus.

19. What are the adverse events associated with the 2nd dose of a varicella vaccine?

According to Canadian Immunization Guide, swelling at the injection site was reported very commonly in young children (i.e., in more than 10% of recipients) after the 2nd dose. A higher incidence of pain, redness and swelling was also reported after the 2nd dose in children less than 13 years of age, compared to the 1st dose.⁷ However, this increase is marginally higher than after the first dose; the incidence of injection site complaints observed <3 days after vaccination was slightly higher after dose 2 (25.4%) than after dose 1 (21.7%). Incidence of systemic clinical complaints was lower after dose 2; fever incidence from days 7–21 was 7% after dose 1 and 4% after dose 2 ($p = 0.009$).⁸

20. What is the incidence of varicella-like rash post the 2nd dose of a varicella vaccine?

In a study using the Merck varicella vaccine in children aged 1 to 12 years old, the incidence of a varicelliform rash after dose 1 was 3%, compared with 1% after dose 2 ($p = 0.008$), with peak occurrence 8–21 days after vaccination.⁸

21. Do children who have laboratory confirmed breakthrough varicella disease require a 2nd dose of a varicella vaccine?

No. Children who have had breakthrough varicella disease after the 1st birthday do not require additional varicella vaccination, whether previously vaccinated or not. Most will not have laboratory confirmation of disease. A physician diagnosis is considered adequate for chickenpox except for mild cases, which are more common in 'breakthrough' varicella (i.e., that occurring in a vaccinated child). Mild cases of varicella should be confirmed by laboratory testing unless there is other evidence that the diagnosis is varicella, such as association with a source case with more typical varicella. Laboratory confirmation of either disease or immunity indicates that the child does not require additional vaccination.

NACI defines vaccine modified (breakthrough) disease as a case of wild type VZV occurring > 42 days after vaccination. Vaccinated children typically tend to have milder cases of disease with fewer lesions, shorter duration of illness and lower incidence of fever.⁵

22. Why is a parent or physician report of breakthrough varicella disease in a child after varicella vaccine not considered proof of immunity?

NACI reports that breakthrough varicella disease after the 1st dose of vaccine is considerably milder than wild type varicella and often presents with an atypical rash of shorter duration.⁵ These factors pose diagnostic challenges for physicians and laboratory confirmation of infection is recommended. If a breakthrough episode is not laboratory confirmed, a child should be offered a 2nd dose of varicella vaccine.

23. Do children with a history of physician diagnosed herpes zoster (shingles) after their 1st dose of varicella vaccine require a 2nd dose?

No, those with physician diagnosed shingles after their 1st dose of varicella vaccine do not require a 2nd dose as shingles is a reactivation of the varicella virus in the body. A clinical diagnosis of shingles by a physician is more accurate than the clinical diagnosis of mild suspected breakthrough chickenpox.

24. Is laboratory testing after the 1st dose of a varicella vaccine useful in determining the need for a 2nd dose?

Laboratory testing is not recommended to determine the need for a 2nd dose of varicella vaccine in children. Commercially available varicella antibody tests may not have sufficient sensitivity to detect antibody after vaccination. Clinical trials have used other antibody assays as a measure of protection. The gpELISA assay is available through the National Microbiology Laboratory in Winnipeg and is used for assessing response to vaccine in immunocompromised hosts. It is not recommended for use in healthy individuals.

25. What is the lifetime risk of developing herpes zoster (shingles) after wild type varicella disease compared to the varicella vaccine?

The lifetime risk of having shingles after wild type varicella disease is estimated to be 15%-20%. The vaccine virus can also reactivate and cause shingles. However, the reactivation rate for shingles in vaccinated persons appears to be less frequent, and the disease less severe than following natural infection. The long-term effect of a 2 dose varicella vaccination program on the incidence of shingles in children and adults is currently unknown, and this will be observed over time. In US surveillance for zoster (shingles), no consistent trends by age have been observed since the implementation of varicella vaccination programs in 1995, almost 10 years earlier than in BC.⁹

26. What is the estimated effectiveness and duration of protection of a 2 dose varicella immunization schedule?

Kuter et al. prospectively followed 2,196 children for breakthrough disease over a 10 year period.¹⁰ These children had received either 1 dose or 2 doses of Varivax™ administered 3 months apart between 12 months and 12 years of age. This study reported a 10 year vaccine effectiveness of 98.3% in children vaccinated with 2 doses. NACI states that the duration of immunity derived from 2 primary doses during childhood, other than the study just cited, is unknown.¹

27. Will children who received 2 doses of varicella vaccine require a booster in adulthood?

The duration of immunity derived from 2 doses of varicella vaccine during childhood and the need for boosters in adulthood is currently unknown. This will be monitored and recommendations changed in the future if warranted. At this time, the 2 doses are deemed adequate for protection. NACI discusses evidence that there is greater humoral and cell-mediated immunity in a 2 dose varicella series when compared to only 1 dose.¹

28. Will the burden of varicella disease be shifted from children to adults with the 2 dose varicella immunization program?

NACI discusses the 2 dose varicella vaccination schedule in children and summarizes study findings.⁵ Overall, the 2 dose program (when compared to 1 dose only) is anticipated to further reduce the burden of varicella disease and related complications in adolescence and adulthood because it will reduce the number of cases of chickenpox and therefore potential sources of infection for susceptible children and adults.

However, the average age of individuals with wild type and breakthrough disease will be higher. The observation of a higher frequency of complications with chickenpox occurring at older ages is expected to be offset by the decrease in disease incidence overall. The impact of the 2 dose varicella program will be monitored over time.

29. Why should special attention be paid to identification of varicella susceptible immigrants from tropical countries?

Adult immigrants new to BC from tropical countries may have a higher rate of susceptibility to varicella disease and its complications. In BC we consider varicella a childhood disease, but in many tropical countries varicella disease is more common among adults. Mandal summarized previous studies where high ambient temperature, epidemiologic interference from other viruses, and race

were hypothesized to be factors in higher varicella disease rates in adults in tropical countries.¹¹ Findings from studies in India indicate that rural residence is associated with higher rates of varicella susceptibility in adulthood than urban residence. Any adult without a prior history of chickenpox should be offered testing, and if non-immune, varicella immunization.

30. Why should special attention be paid to identification of varicella susceptible women of childbearing age?

Varicella infection in pregnancy is associated with congenital varicella syndrome. The overall risk is estimated at 1.1% if infection occurs in the first 20 weeks of pregnancy. As well, a susceptible woman who develops varicella in the peri-partum period can transmit the infection to her susceptible infant, and neonatal disease is more serious than that in older childhood. Immunization of susceptible women prior to pregnancy is preferred as it will provide protection during pregnancy and the peri-partum period, as well as maternally acquired immunity for the infant. Susceptible pregnant women and their newborn infants should seek medical attention promptly if they are exposed to chickenpox.

¹ National Advisory Committee on Immunization. Statement on varicella vaccination two-dose recommendations. Can Comm Dis Rep. 2010; 36(ACS-8):1-26

² Chaves SS, Gargiullo P, Zhang JX et al. Loss of vaccine induced immunity to varicella over time. N Engl J Med. 2007;356(11):1121-1129

³ National Advisory Committee on Immunization. Statement on measles-mumps-rubella-varicella vaccine. Can Comm Dis Rep. 2010; 36(ACS-9):1-22

⁴ Public Health Agency of Canada [Internet]. Ottawa: [updated 2012 Aug 20; cited 2012 Sep 14]. Publicly Funded Immunization Programs in Canada Routine Schedule for Infants and Children including special programs and catch-up programs, June 2012. Available from: <http://www.phac-aspc.gc.ca/im/ptimprog-progimpt/table-1-eng.php>

⁵ National Advisory Committee on Immunization. Literature review on one-dose and two-dose varicella vaccination. Can Comm Dis Rep. 2010; 36(ACS-10):1-24

⁶ Centers for Disease Control and Prevention [Internet]. Atlanta: [updated 2012 Jun 11; cited 2012 Sep 14]. Recommended immunization schedule for persons aged 0 through 6 years United States, 2012. Available from: <http://www.cdc.gov/vaccines/schedules/downloads/child/0-6yrs-schedule-pr.pdf>

⁷ National Advisory Committee on Immunization. Canadian Immunization Guide. 7th ed. Ottawa: Public Health Agency of Canada; 2006

⁸ Ngai AL, Stahle BO, Kuter BJ, et al. Safety and immunogenicity of one vs. two injections of Oka/Merck varicella vaccine in healthy children. *Pediatr Infect Dis J*. 1996;15:49-54

⁹ Advisory Committee on Immunization Practices. Prevention of varicella. *MMWR Recomm Rep*. 2007;56(RR-4):1-48

¹⁰ Kuter B, Matthews H, Shinefield H, Black S, Dennehy P, Watson B, et al. Ten year follow-up of healthy children who received one or two injections of varicella vaccine. *Pediatr Infect Dis J*. 2004; 23(2):132-7

¹¹ Mandal BK, Mukherjee PP, Murphy C, Mukherjee R, Naik T. Adult susceptibility to varicella in the tropics is a rural phenomenon due to the lack of previous exposure. *J Infect Dis*. 1998 Nov;178Suppl 1:S52-4