Rotavirus Vaccine: Questions and Answers for Health Care Providers

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**Table of Contents**

Program Background, Rationale, and Eligibility ................................................................. 3

1. Why is there a rotavirus vaccine program offered in Manitoba? ........................................ 3

2. Which rotavirus vaccine does Manitoba use in the publicly-funded immunization program? .... 3

3. Who qualifies for publicly-funded oral rotavirus vaccine? .................................................. 3

4. Why does the vaccine series need to be completed before 8 months of age? .......................... 3

5. How is the Rotarix™ vaccine packaged? ............................................................................... 4

6. How are the oral tube and cap disposed of after use? ............................................................. 5

7. Can the vaccine virus be spread to others including susceptible household contacts? ............... 6

8. Should a “spit-up” dose of vaccine be repeated? ..................................................................... 6

9. Are there any precautions that health care providers should take when administering the oral rotavirus vaccine? ............................................................................................................ 6

10. Oral rotavirus vaccine contains sucrose in an amount expected to have an effect on immunization injection pain. When should Rotarix™ be given in relation to the injection of other vaccines to elicit a reduction in pain? .................................................................................................................. 6

11. Is additional screening for potential contraindications required prior to administration of rotavirus vaccine? .................................................................................................................. 6

12. Can Rotarix™ be given at the same time as other vaccines? ................................................... 7

13. Are the different rotavirus products (e.g. RotaTeq® (Merck) and Rotarix™ (GSK)) interchangeable? .................................................................................................................. 7

Vaccine Efficacy, Precautions, Safety ...................................................................................... 7

14. What is the duration of protection? .......................................................................................... 7

15. What is the efficacy of rotavirus vaccines? ............................................................................. 7

16. What are the expected side effects of Rotarix™? ................................................................... 8

17. What is intussusception? ......................................................................................................... 8

18. What is the known risk of intussusception following vaccination with Rotarix™? ................. 8

19. Can the vaccine virus be spread to others including susceptible household contacts? ........... 9

20. Are there issues related to circulating maternal antibodies interfering with the response to the live attenuated vaccine? .................................................................................................. 10

21. Is there a duty to inform clients (particularly those who, for religious reasons, do not eat pork) about the presence of porcine circovirus-1 in the vaccine? ............................................................................. 10

22. Should the rotavirus vaccine be postponed if the infant is ill? ............................................. 10

23. Are there special considerations for premature infants? ...................................................... 10

24. Can rotavirus vaccine be given to hospitalized infants? ...................................................... 10

25. Are there special considerations for breastfed infants? ....................................................... 10

26. Should the vaccine be given to a client who has already had rotavirus gastroenteritis? ........ 11

References ................................................................................................................................ 12
Program Background, Rationale, and Eligibility

1. Why is there a rotavirus vaccine program offered in Manitoba?
   Rotavirus vaccine is being offered to protect Manitoba children against a group of gastrointestinal viruses that infects approximately 95% of children worldwide by time they are 5 years of age.
   In Canada, rotavirus infection occurs most often during the winter months, with incidence peaking from March to May.
   Symptoms of rotavirus include approximately 4-8 days of vomiting, profuse watery diarrhea, and fever. These symptoms can range from mild to very severe. Rotavirus gastroenteritis is the most likely type of gastroenteritis to result in hospitalization.
   Children less than 2 years of age have the peak incidence with highest burden of disease and face the most complications (dehydration, electrolyte imbalance and metabolic acidosis). The Canadian Immunization Guide (CIG), states that 36% of infants with rotavirus gastroenteritis will require physician consultation, 15% an emergency room visit, and 7% will require hospitalization.
   Providing rotavirus vaccine will protect infants from getting ill and potentially experiencing serious complications from this illness. It will also decrease parental stress and time off work to care for ill children and decrease health care utilization and costs.

2. Which rotavirus vaccine does Manitoba use in the publicly-funded immunization program?
   Manitoba uses Rotarix™, manufactured by GlaxoSmithKline (GSK).
   Rotarix™ is an ORALLY ADMINISTERED live attenuated human rotavirus vaccine that is approved by Health Canada. It protects against gastroenteritis caused by rotavirus types G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8].

3. Who qualifies for publicly-funded oral rotavirus vaccine?
   Introduced in April 2014, the rotavirus vaccine is offered free of charge as part of Manitoba’s routine childhood immunization schedule for infants at 2 months and 4 months of age. No further doses are given.
   For children who are off the routine recommended schedule, the relevant parameters for timing limitations for the two doses of the vaccine are:
   - the minimum age for receipt of the 1st dose is 6 weeks + 0 days
   - the 1st dose should be given by 15 weeks (14 weeks plus 6 days) of age
   - the minimum interval between the two doses is 4 weeks
   - the two-dose series should be completed by 32 weeks or 8 months of age (8 months less 1 day)
   Note: If the 1st dose is administered at 15 weeks of age or older the remaining series should be completed with a minimum of 4 weeks between each dose and all doses should be administered before 8 months of age.

4. Why does the vaccine series need to be completed before 8 months of age?
   The age limit on the vaccine series completion is related to a lack of safety data on the administration of this vaccine to older infants.
5. How is the Rotarix™ vaccine packaged?

The ORAL tube (shown in the image below) contains 1.5mL of the vaccine which is a clear, colorless fluid.

New providers unfamiliar with this format should be reminded that it is an ORAL application and that the vaccine should NOT BE INJECTED by needle under any circumstances.

It should be kept refrigerated between 2-8ºC and protected from light.

Note: in April 2017 the manufacturer updated the packaging from an oral applicator to a tube.

Image courtesy of GSK Inc.

6. How to administer the Rotarix™ vaccine from the tube?

To minimize the chance of a spit up dose, administer the oral rotavirus vaccine at the beginning of the appointment while the child is happy. This vaccine is given orally – straight from the tube and is ready to use – no mixing is required.

Give the vaccine 1-2 minutes prior to the injection of other vaccines.

Before giving the vaccine:

- Check the expiry date
- Check that the tube has not been damaged or already opened
- Check that the liquid is clear and colourless, without any particles in it
- If you notice anything abnormal, do not use the vaccine and report the issue to the Inventory Management Officer at MHSAL via the Vaccine and Biologic Product Complaint Process (http://www.gov.mb.ca/health/publichealth/cdc/div/docs/vbpcpf.pdf)

Getting the tube ready

1. Pull off the cap
   a. Keep the cap – you need this to pierce the membrane.
   b. Hold the tube upright.
2. Repeatedly flick the top of the tube until it is clear of any liquid.
   a. Clear any liquid from the thinnest section of the tube by flicking just below the membrane.
3. Position the cap to open the tube  
   a. Hold the tube upright  
   b. Hold the side of the tube  
   c. There is a small spike inside the top of the cap – in the centre  
   d. Turn the cap upside down (180°)

4. To open the tube  
   a. You do not need to twist. Press the cap down to pierce the membrane.  
   b. Then lift off the cap.

Check the tube has opened correctly
1. Check the membrane has been pierced  
   a. There should be a hole at the top of the tube.

2. What to do if the membrane has not been pierced  
   a. Return to the previous section and repeat the steps of piercing the membrane with the cap.

Give the vaccine
1. Position the child to give the vaccine  
   a. While being held by the caregiver, seat the child leaning slightly backwards

2. Administer the vaccine  
   a. Squeeze the liquid gently into the side of the child’s mouth – towards the inside of their cheek.
   b. You may squeeze the tube a few times to get all of the vaccine out – it is okay if a drop remains in the tip of the tube.
   c. The sweet taste of the vaccine will likely stimulate the child to swallow the vaccine.

7. How are the oral tube and cap disposed of after use?  
   Use a biological waste container.

8. Should a “spit-up” dose of vaccine be repeated?  
   No. The CIG states that spit up doses should not be re-administered as the safety of administering a repeat dose of rotavirus vaccine is not known. In clinical trials spitting up was rarely seen.
To minimize the chance of a spit up dose, administer the oral rotavirus vaccine first before the child becomes distressed by injections or other procedures following the instructions above.

9. Are there any precautions that health care providers should take when administering the oral rotavirus vaccine?

There are no case reports in the literature of health care providers contracting rotavirus during the process of administering the vaccine.

There are no additional precautions that should be taken when administering the oral rotavirus vaccine. An immune compromised immunizer does not need to take special infection control precautions or avoid handling the vaccine.

Gloves are not recommended for any immunizers. As always, if an immunizer comes into contact with the contents of a vaccine or with bodily fluids they should wash their hands immediately and follow standard precautions and established clinic procedure to clean up any spills on hard surfaces.

10. Oral rotavirus vaccine contains sucrose in an amount expected to have an effect on immunization injection pain. When should Rotarix™ be given in relation to the injection of other vaccines to elicit a reduction in pain?

Though the impact of Rotarix™ on immunization pain has not been studied directly, it contains sucrose in amounts known to provide analgesic benefits. To obtain this effect, it should be given 1-2 minutes prior to the injection of other vaccines. This allows time for the oral vaccine to be absorbed from the mouth, and affect the neurotransmitters in the infant’s brain. As breastfeeding combines multiple additional pain management strategies it should be also encouraged whenever possible, during vaccine injections.

11. Is additional screening for potential contraindications required prior to administration of rotavirus vaccine?

Yes. A routine pre-immunization health assessment should be conducted including questions screening for contraindications specific to rotavirus vaccine such as:

- A severe allergic reaction to a previous dose of Rotavirus vaccine or any contents of the vaccine or its container.
- A history of intussusception
- An uncorrected congenital malformation of the gastrointestinal tract, such as Meckel’s diverticulum, that would predispose the child to intussusception. However, infants with chronic gastrointestinal disease who are not considered immunocompromised are likely to benefit from rotavirus vaccine.
- Any suspected or known immunodeficiency conditions (e.g. severe combined immunodeficiency disorder (SCID)). Given the young age of these clients, it is possible that SCID may be undiagnosed at the time of the appointment. Therefore, to assess for this condition inquire about a family history of SCID or a history of recurrent, unexplained early deaths in the family. This question is designed to solicit information about infants whose deaths were related to immune compromise rather than deaths in healthy infants ruled to be caused by sudden infant death syndrome (SIDS). Clients who identify a family history of either SCID or recurrent unexplained early deaths should see their family physician for assessment and referral to a pediatric immunologist. If there is a
suggested or known immunodeficiency, the child should not be vaccinated until consultation is received.

12. Can Rotarix™ be given at the same time as other vaccines?
   Yes. When other vaccines routinely recommended as part of MB’s routine childhood immunization schedule are given at the same time as rotavirus vaccine, the immune responses and safety are unaffected.
   Rotavirus vaccine can be administered simultaneously or at any interval before or after other live injectable or intranasal vaccines (including BCG vaccine), if indicated with the exception of oral polio virus vaccine. Infants who have received oral polio vaccine should have a 2 week interval before receipt of oral rotavirus vaccine to ensure the immune response to the rotavirus vaccine is unaffected.
   Due to the difference in ages between routinely scheduled doses of rotavirus vaccines in early infancy and MMR and varicella vaccines routinely given at 12 months, it is unlikely that providers will need to co-administer another live attenuated vaccine at the same time as rotavirus vaccine, except in the circumstance of infants being vaccinated with MMR vaccine for travel, which may be done as early as 6 months of age.

13. Are the different rotavirus products (e.g. RotaTeq® (Merck) and Rotarix™ (GSK)) interchangeable?
   There is no data on safety, immunogenicity or efficacy on vaccine interchangeability between the two rotavirus vaccines. Manitoba’s publicly-funded immunization program uses Rotarix™. Given that the two vaccines differ in composition and schedule, whenever possible, the series should be completed with the same product.
   However, if the product used for a previous dose(s) is not known, complete the series with the available product.
   If any prior dose administered is known to be RotaTeq®, a total of 3 doses of vaccine should be administered by 8 months of age.

Vaccine Efficacy, Precautions, Safety

14. What is the duration of protection?
   Efficacy was documented for two rotavirus seasons following immunization. There is no robust data on efficacy after this point (Vesikari, 2010). See question 15.

15. What is the efficacy of rotavirus vaccines?
   Vaccine efficacy against severe disease in developed world settings has been shown to be 74-89%, with efficacy against any rotavirus gastroenteritis at 85-98%.
   In Ontario, when comparing rotavirus-specific gastroenteritis hospitalization post-rotavirus vaccine period to a period before the rotavirus vaccine program there was a 75% decrease in hospitalizations.
   An evaluation provided by the National Enteric Surveillance Program (NESP) in 2017 identified that the rates of rotavirus hospital discharges among infants in Manitoba (less than 12 months of age) declined from approximately 100 cases/100,000 in 2006 (before the publicly-funded rotavirus vaccine program in MB) to 6 cases/100,000 in 2015 (a year after
the implementation of the rotavirus vaccine program). In addition, the rates of rotavirus infection dropped from 6.9 cases/100,000 in 2006 to 2.0 cases/100,000 in 2015.

16. What are the expected side effects of Rotarix™?
Common side effects include diarrhea in the 7 day period after vaccination and vomiting.
Uncommon side effects include dermatitis, abdominal pain, and/or flatulence.
Some post-marketing studies have found an association with intussusception which may occur rarely after vaccination.
Vaccine providers are asked to report adverse events following immunization (AEFI) (http://www.gov.mb.ca/health/publichealth/cdc/div/aefi.html), particularly:
- Intussusception in the first 21 days following any dose of rotavirus vaccine.
- Any serious or unexpected adverse event temporally related to vaccination. An unexpected AEFI is an event that is not listed in available product information but may be due to the immunization, or a change in the frequency of a known AEFI.

17. What is intussusception?
Intussusception occurs when one portion of the bowel slides into the next, much like the pieces of a telescope, creating a blockage in the bowel.
In most infant cases the cause is unknown, but it has been linked with viral infection. It occurs most frequently in babies between the ages of 5 and 10 months at a rate of 34 cases/100,000 per year.
Symptoms are abdominal pain, usually evident because of bouts of persistent crying and the infant drawing up their legs and vomiting. Sometimes blood is seen in the stools. This condition is managed in hospital, where a barium or air enema is used to reverse the blockage. Most cases recover completely with no further problems. Complications can occur if treatment is delayed, and surgery or antibiotics may be needed.
Intussusception can recur in up to 10% of radiologically reduced cases, sometimes within a few days and usually within the next 6 months. For this reason, a history of intussusception is a contraindication to receipt of rotavirus vaccine.

18. What is the known risk of intussusception following vaccination with Rotarix™?
Published data from several countries are suggestive of a small increased risk of intussusception using current rotavirus vaccines.
Intussusception in the first year of life occurs at a rate of 34 per 100,000 per year; however, the rate varies with age in the first year of life and peaks between 5 and 10 months of age.
Surveillance for intussusception following the introduction of routine infant rotavirus immunization programs in several countries suggested a small increased risk of intussusception following rotavirus vaccination. Subsequent epidemiologic studies using different methods have estimated the risk as between 1 and 7 excess cases of intussusception per 100,000 doses in the 7 days following the first and second dose of rotavirus vaccine. The Global Advisory Committee on Vaccine Safety (GACVS) of the WHO reviewed the findings from these studies and noted that the findings remain reassuring; the risk of intussusception following current rotavirus vaccines is small.
The US Advisory Committee on Immunization Practices has reviewed the available data from the above studies and recommends that the benefits of rotavirus vaccines greatly outweigh the potential risks of intussusception in the US population.
The Canadian National Advisory Committee on Immunization (NACI) statement on rotavirus vaccine was updated in 2010 prior to the publication of the recent studies, but NACI has not withdrawn or otherwise modified its recommendations for the routine use of rotavirus vaccines in the infant schedule.

Intussusception rates in rotavirus vaccines have been monitored closely due to previous experience with the RotaShield® vaccine which was withdrawn by Wyeth-Lederle from the US market due to a risk of intussusception estimated at 1 case per 10,000 recipients following the first dose. The estimated risk of intussusception with the two new rotavirus vaccines is much smaller than the risk that was seen with RotaShield®.

In summary, the evidence indicates that intussusception can occur as a result of vaccination with either Rotateq® or Rotarix™ but that the risk is low, on the order of approximately 1 to 7 cases/100,000 doses.

19. Can the vaccine virus be spread to others including susceptible household contacts?

The vaccine virus is excreted in stool for at least 10 days after vaccination. The virus is detected in approximately 50% of stools after the 1st dose and 7-18% of stools after the 2nd dose.

The theoretical risk of vaccine virus transmission should be balanced against the protection the vaccine provides against wild type rotavirus gastroenteritis, which results in attack rates of 47% among susceptible household contacts.

All household contacts, regardless of their immune status should be advised to wash their hands thoroughly after changing diapers. Since the risk of vaccine virus transmission and subsequent vaccine virus-derived disease is reported to be less than the risk of wild type rotavirus transmission, infant vaccination should be encouraged in households containing immunocompromised persons (Anderson, 2008).

Transmission of the vaccine virus from immunized infants has been found to occur between infants/children. The frequency is not widely quantified but is thought to be much less frequent than with wild type virus. One author reported a ~18.8% (95% confidence interval: 10.9%–29.2%) transmission rate between twins (one vaccinated, one unvaccinated) (Han, 2009, as reported in Payne et al., 2010).

No case reports describing the risk of transmission to adults caring for infants were found in a search of the literature (Anderson, 2008).

There is no evidence that rotavirus is a teratogen. Pregnant women are unlikely to become infected with the vaccine virus if hand washing precautions are taken, and because most adults have some pre-existing immunity to rotavirus. Attention to hand hygiene after vaccination is recommended including following changing diapers of babies who have been vaccinated or preparing food in settings where vaccinated infants are present such as day nurseries. These are routine recommendations for such practices because of the risk of fecal oral transmission of human stool pathogens.
20. Are there issues related to circulating maternal antibodies interfering with the response to the live attenuated vaccine?
Studies have not identified interference with circulating maternal antibodies as an issue in vaccine antibody response. The rotavirus vaccines provide comparable protection against laboratory confirmed rotavirus infection in both breastfed and formula fed infants.

21. Is there a duty to inform clients (particularly those who, for religious reasons, do not eat pork) about the presence of porcine circovirus-1 in the vaccine?
No. While fragments of porcine circovirus (PCV)-1 and -2 DNA have been found in the vaccine, these viruses contain no pig or other animal material. Receiving the vaccine would not contravene religious practices.
Clients who have questions can be made aware that while porcine circovirus fragments are considered to be a contaminant in these vaccines, they are not known to cause illness in humans. Health Canada states that there is no evidence that the presence of PCV-1 or PCV-2 in rotavirus vaccines poses a safety risk to recipients (http://www.hc-sc.gc.ca/dhp-mps/brgtherap/activit/fs-fi/rotavirus-questions-eng.php#q10).

22. Should the rotavirus vaccine be postponed if the infant is ill?
As with other vaccines, administration of the rotavirus vaccine should be postponed in infants suffering from acute febrile illness or moderate to severe diarrhea and vomiting until their condition improves unless postponing will result in scheduling of the first dose after 15 weeks of age. However, the presence of a minor infection such as a cold or mild gastroenteritis should not result in the deferral of the vaccination.

23. Are there special considerations for premature infants?
As with all vaccines, this vaccine should be given according to chronological (non-adjusted) age. The same schedule and precautions and contraindications should be used as in full term infants.

24. Can rotavirus vaccine be given to hospitalized infants?
Age-eligible infants should receive the vaccine only at the time of hospital discharge to prevent possible transmission of vaccine strain rotavirus to other hospitalized infants. However, the same timelines for administration must be followed.

25. Are there special considerations for breastfed infants?
No. There are no restrictions on the infant’s consumption of food or liquid, including breast milk, either before or after receipt of oral rotavirus vaccine. The efficacy of the rotavirus vaccine series is similar among breastfed and non breastfed infants.
Breastfeeding mothers should be encouraged to feed babies during immunization injections given at the same visit and following rotavirus vaccine as part of a comprehensive immunization injection pain reduction strategy.
26. **Should the vaccine be given to a client who has already had rotavirus gastroenteritis?**

Yes. The majority of rotavirus infections are not laboratory confirmed and therefore whether or not that an infant has had rotavirus infection is unknown. However, those who have confirmed rotavirus infection in the past should be vaccinated according to the routine schedule because initial infection with rotavirus provides only partial immunity.
References