



ROTAVIRUS VACCINES FOR AUSTRALIAN CHILDREN: INFORMATION FOR GPS AND IMMUNISATION PROVIDERS

Summary

- Rotavirus is the most common cause of severe gastroenteritis in infants and young children, accounting for at least half of all hospitalised cases of gastroenteritis in children less than 5 years of age.
- Two oral live attenuated rotavirus vaccines have been available in Australia since mid 2006. They are Rotarix® (given in a 2 dose schedule at 2 and 4 months of age) and RotaTeq® (given in a 3 dose schedule at 2, 4, and 6 months of age).
- Rotavirus vaccines will be available on the National Immunisation Program (NIP) commencing July 2007 (for babies born from 1 May 2007).
- Vaccination will reduce the risk of developing severe rotavirus gastroenteritis (by ~85–100%) and any rotavirus gastroenteritis (by ~70%).
- Immunisation of older children is not routinely recommended at this time.

Rotavirus

Rotaviruses are RNA viruses that have a characteristic wheel-like appearance when viewed by electron microscopy (the name rotavirus is derived from the Latin *rota*, meaning “wheel”). An Australian researcher, Professor Ruth Bishop, and colleagues originally described rotaviruses as the cause of infant gastroenteritis in 1973.¹ There are a number of different strains of rotavirus, classified by the “G” and “P” outer proteins on the virus. Five strains (G1, G2, G3, G4 and G9) have accounted for around 90% of the serotypes seen worldwide and in Australia.²

Rotaviruses are transmitted by the faecal-oral route. Large numbers of viral particles are shed in faecal matter and the virus is stable in the environment, so contamination of hands and objects (fomites) is relatively easy. Such routes of infection are common in day care centres, family homes, and homes for the elderly. In addition, virus excretion can occur in individuals without symptoms.²

Epidemiology of Rotavirus Disease

Rotavirus is the leading cause of severe acute gastroenteritis in infants and young children. Rotavirus is found in all countries, and almost every child in the world will suffer at least one infection by the time they are 3 years old. An estimated 600,000 children worldwide die each year from rotavirus gastroenteritis, 80 percent of whom live in developing countries. Worldwide, rotavirus causes nearly 2 million hospitalisations each year.³

In Australia, it is estimated that there are approximately 10,000 hospitalisations due to rotavirus in children less than 5 years of age each year, with rotavirus accounting for around half the hospitalisations for any acute gastroenteritis in this age group.^{4,5} This translates to ~4% of children (1 in 27) being hospitalised with rotavirus gastroenteritis by the age of 5 years. In addition to hospitalised children, an estimated 115,000 children under 5 years of age visit a GP, and 22,000 children require an Emergency Department visit.^{4,6} On average, there is one death recorded as due to rotavirus each year in Australia.⁶ Indigenous Australian infants and children are hospitalised with rotavirus gastroenteritis about 3–5 times more commonly than their non-Indigenous peers.^{7–9} Rotavirus infections follow a seasonal pattern in temperate Australia with peak incidence in mid to late winter. In the northern tropical and arid regions of Australia, there is no consistent seasonal pattern and disease peaks are unpredictable.⁸

Clinical Characteristics of Rotavirus Disease

Children can be infected with rotavirus several times during their lives. The spectrum of illness ranges from mild, watery diarrhoea of limited duration to severe dehydrating diarrhoea with vomiting and fever, which can result in death. The clinical features of rotavirus gastroenteritis are non-specific so diagnosis can only be confirmed by laboratory testing of faecal specimens. Infections occurring in the first few months of life are generally asymptomatic.¹⁰ The peak incidence of rotavirus disease causing severe diarrhoea and dehydration is between 6 and 24 months of age² but disease occurs earlier in Indigenous children in the Northern Territory.

Rotavirus Vaccines

Two rotavirus vaccines have been available on the private market since May 2006. In March 2007, the Australian Government announced that rotavirus vaccines would be funded under the NIP commencing in July 2007 for babies born after 1 May 2007. Immunisation providers should consult their State or Territory Health Department for details of the program in their locality.

The two oral rotavirus vaccines available are **RotaTeq**[®] (CSL Biotherapies/Merck & Co, Inc) and **Rotarix**[®] (GlaxoSmithKline). There are differences in the composition and number of doses required of each vaccine. RotaTeq[®] is a human-bovine reassortant vaccine containing five vaccine viruses (types G1, G2, G3, G4 and P1a[8]). Rotarix[®] vaccine contains a single, attenuated human rotavirus of serotype G1P1a[8]. Both vaccines have been shown to have similar efficacy against rotavirus gastroenteritis of any severity of around 70%. The efficacy against severe rotavirus gastroenteritis is higher and ranged from 85% to 100% in clinical trials in many different countries.¹¹⁻¹³ Overall, the vaccines prevented around half (42%–58%) of all hospital admissions for acute gastroenteritis of any cause in young children,¹¹⁻¹³ suggesting that rotavirus is responsible for a greater proportion of severe gastroenteritis than previously recognised.

Rotavirus vaccines are administered orally at the same time as the other vaccines on the childhood immunisation schedule at either 2, 4 and 6 months of age (RotaTeq[®]), or 2 and 4 months of age (Rotarix[®]). The interval separating the doses should be no less than 4 weeks.^{14,15} The ages of administration at which the rotavirus vaccines are registered for use in Australia are shown in Table 1, adapted from the draft 9th edition of *The Australian Immunisation Handbook*.¹⁶ It is important for immunisation providers and parents to note that unlike other NIP vaccines, there are *upper* limits for the administration of both the first and final doses of rotavirus vaccines.

Table 1: Age limits for administration of oral Rotavirus vaccines

	Number of Doses	Age of routine administration	Age limits for dosing			Minimum interval between doses
			1 st dose	2 nd dose	3 rd dose	
Rotarix [®] (GlaxoSmithKline)	2 oral doses (1 mL/dose)	2 and 4 months	6–14* weeks	10–24* weeks	None	4 weeks
RotaTeq [®] (CSL Biotherapies/ Merck & Co Inc)	3 oral doses (2 mL/dose)	2, 4 and 6 months	6–12† weeks	10–32† weeks	14–32† weeks	4 weeks

* The upper age limit for receipt of the first dose of Rotarix is 14.9 weeks, that is up to the anniversary of the 15th week of age. The upper age limit for receipt of the second dose of Rotarix is 24.9 weeks, that is up to the anniversary of the 25th week.

† The upper age limit for receipt of the first dose of RotaTeq is 12.9 weeks, that is up to the anniversary of the 13th week of age. The 2nd dose of vaccine should preferably be given by 28 weeks of age to allow for minimum interval of 4 weeks prior to receipt of 3rd dose, and the upper age limit for either the second or third doses is 32.9 weeks, that is by the anniversary of the 33rd week.

Co-administration with other vaccines

Rotavirus vaccines can be co-administered with other vaccines on the NIP. Evidence from clinical trials suggests that co-administration of oral rotavirus vaccines is safe and does not interfere with the immune response of the other vaccine antigens. Although co-administration of rotavirus vaccines with BCG has not been assessed in clinical trials there is unlikely to be any interference between the two vaccines and they can be co-administered at any time in relation to one another.

The Safety of Rotavirus Vaccines

The currently licensed rotavirus vaccines have undergone some of the largest and most stringent testing in clinical trials ever seen for any vaccine. This has in part been because of the concerns regarding the previous vaccine called RotaShield[®], licensed in the United States in 1998/99. Approximately 1 million children were vaccinated over a 9 month period of whom about 100 developed a type of bowel obstruction called intussusception resulting in withdrawal of Rotashield[®] from the USA market. However, intussusception occurs for unknown reasons in about 1 child per 10,000, in the absence of any vaccine, most often in infants aged 4 to 10 months. There is still some uncertainty about the overall magnitude of the relationship between Rotashield[®] and intussusception, with the strongest association with the first dose, particularly if it was given over the age of 3 months.¹⁷ For this reason, the clinical trials of Rotarix[®] and RotaTeq[®] limited administration of the first dose of vaccine to infants under 3 months of age, and did not give subsequent doses to children past a certain age (6 months [24 weeks] for Rotarix[®] and ~7.5 months [32 weeks] for RotaTeq[®]).^{11,12}

The current rotavirus vaccines (RotaTeq[®] and Rotarix[®]) differ in composition to RotaShield[®] and the clinical trials conducted prior to licensure had enough participants to exclude an increased risk of intussusception in vaccine recipients comparable to that with RotaShield[®]. However, as these trials did not test the vaccines in older infants the current vaccines are not licensed for use above the age limits stated. When there is additional experience in large numbers of infants, the current upper age limits specified in the product information/s (and in Table 1) may be relaxed. In the meantime providers may wish to discuss with parents the risks and benefits of giving vaccine doses outside the strict age limits for children with conditions putting them at increased risk of severe rotavirus disease.¹⁶

Vaccine recipients may have a slightly increased risk (1–3%) of developing diarrhoea or vomiting in the week after vaccine administration. The incidence of fever, irritability, and other adverse events was not different in vaccine recipients as compared with placebo recipients in clinical trials.^{11,12,16,18}

Why is catch-up immunisation or primary immunisation of older infants and children not suggested?

The three main reasons why catch-up immunisation or immunisation of older children is not considered appropriate are: (1) the theoretical concerns regarding intussusception (discussed above); (2) lack of data in older infants or children; and (3) the main burden of rotavirus disease is in children less than 3 years of age. Older children are usually protected from developing severe disease due to rotavirus because they have acquired partial immunity from being infected earlier in life.^{2,19} Unlike other childhood diseases, such as measles and chickenpox, natural rotavirus infection doesn't offer lifetime protection, but provides protection from severe disease when subsequently exposed to the virus. Rotavirus vaccines provide similar protection to natural infection, but without causing disease along the way.² Similarly, vaccination of adults is not recommended because it is likely that they may have partial pre-existing immunity and are unlikely to experience severe rotavirus disease.

What happens if a vaccine dose is given inadvertently to an older infant or child?

There are no data regarding the use of the current rotavirus vaccines in older infants and children, although it is likely that the safety profile will be similar to younger infants. Extensive post-market surveillance of rotavirus vaccines is being undertaken in studies in a number of countries and will, over time, provide information regarding the "off label" use of rotavirus vaccines.



Contraindications, Precautions and Special Considerations

Contraindications

- Rotavirus vaccine should not be given to any infant who has hypersensitivity to any component of the vaccine or who has had an anaphylactic reaction to a previous dose of either vaccine.
- As recommended for all vaccines, rotavirus vaccine should not be given during any moderate to severe febrile illness (see *Precautions*).^{14,15}

Precautions

- Infants with pre-existing chronic gastrointestinal conditions (such as congenital malabsorption syndrome, Hirschsprung's disease, short-gut syndrome) are at risk of more severe disease from rotavirus and so stand to benefit more from vaccination. However, neither safety nor efficacy of vaccination has been established for infants with such conditions. Providers should consider the potential risks and benefits of administering rotavirus vaccine to such infants.^{16,18}
- Rotavirus vaccination is not recommended for infants who have known or suspected immunodeficiency. Neither the safety nor efficacy of vaccination has been established for infants with such conditions.¹⁸ However, the household contacts of immunodeficient patients can be vaccinated (see *Special Considerations*).
- Infants with an acute moderate to severe illness, including acute gastroenteritis, should not be vaccinated until their condition has improved. However, infants with mild gastroenteritis can be vaccinated.¹⁸

Special considerations

- Infants living in households with persons who have or are suspected of having an immunodeficiency disorder or impaired immune status can be vaccinated.¹⁸ Vaccine rotaviruses can be shed in the stool of vaccine recipients after administration (particularly the first dose). However, the protection of the immunocompromised household member afforded by vaccination of young children in the household outweighs the small risk for transmitting vaccine virus to the immunocompromised household member and any subsequent theoretical risk for vaccine virus-associated disease.^{16,18}
- Infants living in households with pregnant women can be vaccinated.¹⁸
- There are limited data on the use of rotavirus vaccine in premature infants. Vaccination of premature infants according to chronological age is recommended if they are at least 6 weeks of age and are clinically stable.^{16,18}
- Administration of oral rotavirus vaccines to hospitalised infants has not been studied in clinical trials. Both rotavirus vaccines are shed in the stool, particularly following the first dose. However, studies looking at horizontal transmission (ie. person to person spread) have not been performed. If hospitalised infants are otherwise clinically stable and at the appropriate chronological age, administration of rotavirus vaccines in the hospital setting can be considered, particularly if delaying the dose would preclude completing the immunisation schedule on time.¹⁶
- Re-administration of a dose of rotavirus vaccine is not necessary if infants have regurgitated or spat out the vaccine after administration,¹⁶ however, immediate redosing is appropriate if it appears that all or most of the dose has been regurgitated. There have been no studies performed to assess re-dosing.^{14,15,18}

Interchangeability of Rotavirus Vaccines

There are no studies that address the interchangeability of the two available rotavirus vaccines. Completion of a vaccination course should be with rotavirus vaccine from the same manufacturer whenever possible. However, under the NIP, the vaccines provided in each State/Territory differ with Rotarix[®] currently being used in the Australian Capital Territory, New South Wales, the Northern Territory, Tasmania and Western Australia, and RotaTeq[®] in Queensland, South Australia and Victoria. In the setting where an infant moves to a jurisdiction where the different vaccine is funded, and has not completed the course of vaccination as recommended in their S/T, the following approach is suggested. Because RotaTeq[®] is given in a 3-dose schedule, if either dose 1 or 2 of vaccine is given as RotaTeq[®], a third dose of either rotavirus vaccine should be given, provided that the upper age limit for that dose and inter-vaccine interval (4 weeks between any doses) are met. Parents/providers can be counselled that in the event that fewer doses than the recommended number have been administered, it is still likely that partial protection against rotavirus disease has been provided.

Advice to Parents

Rotavirus vaccine is the best way to protect children against rotavirus disease. The vaccine will not prevent diarrhoea and vomiting caused by other infectious agents but is very good at preventing severe diarrhoea and vomiting caused by rotavirus, which causes about half of all episodes of hospitalised gastroenteritis in infants and young children. Both vaccines are about 70% protective against any rotavirus gastroenteritis, and between 85%–100% effective in preventing severe rotavirus gastroenteritis. Children who receive the rotavirus vaccine are less likely to be hospitalised, visit the Emergency Department, or see a doctor for gastroenteritis.^{11,12,18}

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