

Rotavirus

ROTAVIRUS VACCINES FOR AUSTRALIAN CHILDREN: INFORMATION FOR IMMUNISATION PROVIDERS

Disease and epidemiology

- Rotavirus is the most common cause of acute severe gastroenteritis in children <5 years old.
- Approximately 500,000 deaths due to rotavirus occur each year, predominantly in developing countries.
- Approximately 10,000 hospitalisations and 22,000 Emergency Department visits due to rotavirus occur in children <5 years of age in Australia each year. This represents approximately half of all the hospitalised cases of acute gastroenteritis in children <5 years of age in Australia.
- Vaccination is anticipated to reduce the risk of developing severe rotavirus gastroenteritis requiring hospitalisation by ~85–100% and any rotavirus gastroenteritis by ~70%.

Who should be vaccinated

- Rotavirus vaccines are recommended and funded under the National Immunisation Program (NIP) for routine immunisation of Australian infants in the first year of life, in either a 2- or 3-dose course starting from around 2 months of age.
- Immunisation of older children or adults is not recommended.

Vaccines

- Two oral live attenuated rotavirus vaccines are available in Australia. They are Rotarix[®], a human monovalent vaccine (given in a 2-dose schedule at 2 and 4 months of age), and RotaTeq[®], a pentavalent human bovine reassortant vaccine (given in a 3-dose schedule at 2, 4 and 6 months of age).
- Rotavirus vaccines first became available in early 2006, and were added to the NIP from 1 July 2007 (for babies born from 1 May 2007).
- Upper limits on the recommended age of administration of rotavirus vaccines are in place.

The disease

Rotavirus is an RNA virus that has 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 quite stable in the environment, so

contamination of hands and objects (fomites) is relatively easy. These routes of transmission are common in day-care centres, family homes, and homes for the elderly. In addition, virus excretion can occur in individuals without symptoms.²

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.³

Epidemiology

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 500,000 children worldwide die each year from rotavirus gastroenteritis, most of whom live in developing countries. Worldwide, rotavirus causes nearly 2 million hospitalisations each year.⁴

The peak incidence of severe rotavirus disease in Australia is between 6 and 24 months of age² but peak disease incidence occurs at an earlier age in Aboriginal and Torres Strait Islander children, particularly those in the Northern Territory.

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

Who should be vaccinated

National Immunisation Program (NIP)

Two rotavirus vaccines became available in Australia on the private market in May 2006. Rotavirus vaccination commenced for all infants in the Northern Territory in October 2006, and in the remaining jurisdictions from 1 July 2007 under the NIP.

Rotavirus vaccines are only recommended for use in young infants. The vaccines are given at either 2 and 4 months of age (Rotarix[®], 2-dose schedule) or at 2, 4 and 6 months of age (RotaTeq[®], 3-dose schedule).

Immunisation providers should consult their state or territory Health Department for details of the program in their locality, as the jurisdictions vary in which vaccine they use. At the time of writing, Rotarix[®] was used in the Northern Territory, New South Wales, Tasmania, the ACT, and Western Australia (until May 2009). RotaTeq[®] is used in Victoria, South Australia, Queensland and Western Australia (from May 2009).

Others

Use of rotavirus vaccine in older children and adults is not recommended (see 'Other considerations' below).

Unlike other routine childhood vaccines, there are upper age limits on the administration of rotavirus vaccines (see 'Vaccines, Administration' below). In addition, on a population basis, most older children and adults will have partial immunity to rotavirus disease based on being previously infected (or immunised) at a younger age (see 'Other considerations' below).

Vaccines

The two oral rotavirus vaccines available are **Rotarix[®]** (GlaxoSmithKline) and **RotaTeq[®]** (CSL Biotherapies/Merck & Co. Inc.). There are differences in the composition and number of doses required of each vaccine. Rotarix[®] vaccine contains a single, attenuated human rotavirus of serotype G1P1a[8]. RotaTeq[®] is a human-bovine reassortant vaccine containing five vaccine viruses (types G1, G2, G3, G4 and P1a[8]).

Administration

Rotavirus vaccines are administered orally at the same time as the other vaccines on the childhood immunisation schedule at either 2 and 4 months of age (Rotarix[®]) or 2, 4 and 6 months of age (RotaTeq[®]). The interval separating the doses should be no less than 4 weeks.^{11,12} The ages of administration for which the rotavirus vaccines are registered for use in Australia are shown in Table 1.¹³ 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 1st and final doses of rotavirus vaccines. If the 1st dose of rotavirus vaccine is

not provided by the specified age, the vaccine course should not be started.

Age limits for dosing of oral rotavirus vaccine

	Doses	Age of routine oral administration	Age limits for dosing			Minimum interval between doses
			1st dose	2nd dose	3rd 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 1st dose of Rotarix[®] is 14.9 weeks, that is up to the anniversary of the 15th week of age, and the upper age limit for receipt of the 2nd dose of Rotarix[®] is 24.9 weeks, that is up to the anniversary of the 25th week of age.

† The upper age limit for receipt of the 1st 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 a minimum interval of 4 weeks before receipt of the 3rd dose, and the upper age limit for either the 2nd or 3rd doses is 32.9 weeks, that is by the anniversary of the 33rd week of age.

Vaccine efficacy/effectiveness

Both rotavirus 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.¹⁴⁻¹⁶ Overall, the vaccines prevented around half (42–58%) of all hospital admissions for acute gastroenteritis of any cause in young children,¹⁴⁻¹⁶ suggesting that rotavirus is responsible for a greater proportion of severe gastroenteritis than previously recognised.

Preliminary evidence from the United States suggests that there has been a significant decline in rotavirus cases in that country since the introduction of rotavirus vaccine onto their immunisation schedule in 2006.¹⁷ There is also early evidence of an impact of the rotavirus program in Australia, suggesting a decline in rotavirus notifications and positive tests in Queensland.^{18,19}

Vaccine safety

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 a previous rotavirus vaccine called RotaShield[®], which was licensed in the United States in 1998/99. In that country, in the approximately 1 million children who were vaccinated over a 9-month period, about 100 developed a type of bowel obstruction called intussusception. This resulted in withdrawal of RotaShield[®] from the USA market, with

subsequent studies suggesting that there was an increased risk of intussusception in vaccine recipients.

Intussusception occurs for unknown reasons in about 1 child per 10,000, in the absence of any vaccine, and is most common in infants aged 4–10 months. There is still some uncertainty about the overall magnitude of the relationship between RotaShield[®] and intussusception; the strongest association was with the 1st dose, particularly if it was given over the age of 3 months.^{20,21} For this reason, the clinical trials of Rotarix[®] and RotaTeq[®] limited administration of the 1st 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[®]).^{14,15}

The current rotavirus vaccines (Rotarix[®] and RotaTeq[®]) 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 seen 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 vaccines' product information (and in Table 1) may be relaxed.

Post-licensure monitoring of the two currently used rotavirus vaccines is being conducted in the United States, Australia and other countries. To date, no vaccine

associated increase in risk of intussusception (or other serious advent) has been detected.^{18,22,23}

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.^{13-15,24,25}

Contraindications/precautions

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’ below).^{11,12}

Precautions

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.^{24,25}

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.^{13,24,25}

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.^{24,25} However, the household contacts of immunodeficient patients can be vaccinated (see below).

Infants living in households with persons who have or are suspected of having an immunodeficiency disorder or impaired immune status can be vaccinated.^{24,25} Vaccine rotaviruses can be shed in the stool of vaccine recipients after administration (particularly the 1st 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.^{13,24,25}

Infants living in households with pregnant women can be vaccinated.^{24,25}

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.^{13,24,25}

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 1st dose. However, studies looking at horizontal transmission (i.e. 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.¹³

Concomitant administration

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 to 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.

Interchangeability

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. 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 the jurisdiction they are leaving, 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 3rd 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.

Other considerations

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 <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.^{2,26} 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-marketing 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.

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% and 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.^{14,15,24,25}

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