



## **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, causing around half of all hospitalised cases of gastroenteritis in children less than 5 years of age.**
- **Two oral live attenuated rotavirus vaccines are available in Australia. They are Rotarix<sup>®</sup> (given in a 2 dose schedule at 2 and 4 months of age) and RotaTeq<sup>®</sup> (given in a 3 dose schedule at 2, 4, and 6 months of age).**
- **Immunisation of older infants or children is not recommended.**
- **Vaccination will reduce the risk of developing severe rotavirus gastroenteritis (by ~ 85–100%) and any rotavirus gastroenteritis (by ~ 70%).**

### **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.<sup>1</sup> There are a number of different strains of rotavirus, which are 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.<sup>2</sup>

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.<sup>2</sup>

### **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.<sup>3</sup>

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.<sup>4,5</sup> This translates to 3.75% 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.<sup>4,6</sup> On average, there is one death due to rotavirus each year in Australia.<sup>6</sup> Indigenous Australian infants and children are hospitalised with rotavirus gastroenteritis about 3–5 times more commonly than their non-Indigenous peers.<sup>7,8</sup> 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.<sup>8</sup>

## Clinical Characteristics of Rotavirus Disease

Children can be infected with a 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 generally non-specific and confirmation of rotavirus infection can only be made by laboratory testing of faecal specimens. Infections occurring in the first 3 months of life are generally asymptomatic.<sup>9</sup> The peak incidence of rotavirus disease causing severe diarrhoea and dehydration is between 6 and 24 months of age.<sup>2</sup>

## Rotavirus Vaccines

Two rotavirus vaccines were registered for use in Australia in early 2006 and have become available on the private market since May 2006. They are both oral vaccines containing live attenuated rotavirus strain(s) and are registered for use in infants only. The cost for a course of immunisation with rotavirus vaccine ranges from \$220 to more than \$350 when purchased at a pharmacy. Rotavirus vaccines are not currently funded under the National Immunisation Program (NIP) (August 2006).

The vaccines are **RotaTeq**<sup>®</sup> (CSL Limited/Merck and Co, Inc) and **Rotarix**<sup>®</sup> (GlaxoSmithKline). There are differences in the composition and number of doses required of each vaccine. RotaTeq<sup>®</sup> is a human-bovine reassortant vaccine containing five vaccine viruses (types G1, G2, G3, G4 and P1a[8]). Rotarix<sup>®</sup> 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.<sup>10-12</sup> Overall, the vaccines prevented around half (42%–58%) of all hospital admissions for acute gastroenteritis of any cause in young children.<sup>10-12</sup>

Rotavirus vaccine can be administered at the same time as the other vaccines on the childhood immunisation schedule at either 2, 4 and 6 months of age (RotaTeq<sup>®</sup>), or 2 and 4 months of age (Rotarix<sup>®</sup>). The interval separating the doses should be no less than 4 weeks.<sup>13,14</sup> The ages of administration at which the rotavirus vaccines are registered for use in Australia are shown in Table 1.

**Table 1:**

	Doses	Age of routine administration	Age limits for dosing (age in weeks)	Minimum interval between doses
RotaTeq <sup>®</sup> (CSL/Merck)	3 oral doses (2 ml / dose)	2, 4 and 6 months	1 <sup>st</sup> dose by 12 weeks 3 <sup>rd</sup> dose by 32 weeks	4 weeks
Rotarix <sup>®</sup> (GlaxoSmithKline)	2 oral doses (1 ml / dose)	2 and 4 months	1 <sup>st</sup> dose by 14 weeks 2 <sup>nd</sup> dose by 24 weeks	4 weeks

## 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 previously licensed vaccine called RotaShield<sup>®</sup>. The Rotashield<sup>®</sup> vaccine was licensed in the United States in 1998/9 and approximately 1 million children were vaccinated over a 9 month period. Of the children who received the vaccine, about 100 developed a type of bowel obstruction called intussusception. However, intussusception occurs for unknown reasons in about 1 child per 10,000, regardless of whether or not they have received any vaccine, and it most often occurs in infants 4 to 10 months of age. Nevertheless, Rotashield<sup>®</sup> was promptly withdrawn from the US market in 1999.



There is still some uncertainty about the relationship between Rotashield<sup>®</sup> and intussusception, but it has been suggested that when the first dose was given to infants over the age of 3 months, the risk of intussusception was increased.<sup>15</sup> For this reason, the clinical trials of Rotarix<sup>®</sup> and RotaTeq<sup>®</sup> 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 for Rotarix<sup>®</sup> and 7.5 months for RotaTeq<sup>®</sup>).<sup>10,11</sup> That is, safety of the current vaccines was not studied in older infants or children.

The current rotavirus vaccines (RotaTeq<sup>®</sup> and Rotarix<sup>®</sup>) differ in composition to RotaShield and in the clinical trials conducted prior to licensure there were enough participants to determine that there was not an increased risk of intussusception in vaccine recipients as compared with placebo recipients. However, as stated above, these trials did not test the vaccines in older infants. When there is additional experience in large numbers of infants with these vaccines the current upper age limits specified in the product information (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.

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.<sup>11,16</sup>

### **Why is catch-up immunisation or primary immunisation of older children not suggested?**

The two main reasons why catch-up immunisation or immunisation of older children is not suggested are: (1) the potential safety concerns regarding intussusception (discussed above); and (2) because 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 partial immunity acquired from being infected earlier in life.<sup>2,17</sup> 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.<sup>2</sup>

### **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*).<sup>13,14</sup>

#### *Precautions*

Rotavirus vaccination may benefit infants with pre-existing chronic gastrointestinal conditions (such as congenital malabsorption syndrome, Hirschsprung's disease, short-gut syndrome). However, neither the 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.<sup>16</sup>

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.<sup>16</sup> However, 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.<sup>16</sup>

### 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.<sup>16</sup> 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.<sup>16</sup>
- Infants living in households with pregnant women can be vaccinated.<sup>16</sup>
- There is limited data on the use of rotavirus vaccine in premature infants. The US Advisory Committee on Immunization Practices (ACIP) supports vaccination of premature infants if they are at least 6 weeks of age, are clinically stable, and have been discharged from hospital.<sup>16</sup>
- Re-administration of a dose of rotavirus vaccine is not recommended if infants have regurgitated or spat out the vaccine after administration.<sup>13,14,16</sup>

### 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. Should a second or third vaccine dose be inadvertently given with vaccine from a different manufacturer, first principles, in the absence of data, would suggest a conservative approach. That is, if a second dose of Rotarix<sup>®</sup> is given following a first dose of RotaTeq<sup>®</sup>, give third dose of RotaTeq<sup>®</sup>. If a second dose of RotaTeq<sup>®</sup> is given following a first dose of Rotarix<sup>®</sup>, give third dose of RotaTeq<sup>®</sup>, provided upper age limit and inter-vaccine interval criteria, as defined above, can be met.

### 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.<sup>10,11,16</sup>

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