19 Rotavirus

VACCINE INTRODUCED IN 2016

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

Introduction

Rotaviruses (RV) belong to the Reoviridae family of viruses. They are composed of double-stranded RNA in a three-layer protein capsid. The two outer capsid proteins are used to classify rotavirus strains into P (protease-sensitive) and G (glycoprotein) serotypes. There are at least seven antigenic groups, A-G. Five serotypes of Group A (G1P, G2P, G3P, G4P and G9P) cause over 90% of clinical rotavirus disease in temperate climates. A change in the major circulating serotype typically occurs every two to three years.

Worldwide, rotaviruses are the commonest cause of community-acquired gastroenteritis in children. According to WHO estimates in 2013 about 215,000 children aged <5 years die each year from rotavirus infections; the vast majority of these children live in change to low-resource countries and over two million children are hospitalised each year with pronounced dehydration. Approximately 37 percent of childhood diarrhoeal deaths and 3.4 percent of all deaths in children under five are due to rotavirus infection.

Children under five years of age, especially those between 6 months and two years are most vulnerable to the disease. Death from rotavirus infection is very rare in countries where there is ready access to oral and parenteral rehydration.

Chapter 19 Rotavirus

After implementation of rotavirus vaccines in childhood immunisation programmes, there has been an over 90% reduction of rotavirus hospitalisations in industrialised and low-resource countries.

Epidemiology

The virus is very infectious; up to ten million viral particles can be excreted per ml. of faeces, and only ten particles are required to cause infection. Spread is predominantly by person-to-person contact or from contaminated environmental surfaces, but infection can be transmitted by the respiratory route, and through contaminated water and food.

Animal to human transmission appears to be rare. Viruses may survive on hands for more than four hours, on environmental surfaces for days to weeks, and in recreational or drinking water for weeks.

The incubation period is from 1-4 days with the peak incidence of infection occuring between 4 and 36 months of age and in winter and spring. Virtually all children throughout the world have been infected with RV by the time they are 5 years old, regardless of socioeconomic or environmental conditions. Infection is rare in those under 2 months of age, because of passively transferred maternal antibody; if infection does occur it is often asymptomatic or mild. However, a small number of infants aged <2 months can develop severe gastroenteritis.

A single infection gives >85% protection against severe rotavirus gastroenteritis, >75% protection against any rotavirus gastroenteritis, and >35% protection against rotavirus infection. Children may have multiple RV infections during the first years of life, with symptoms lessening in severity with each infection. Adults, especially the elderly, can develop rotavirus disease.

Different countries in Europe report widely different rates of disease and of admission to hospital because of RV disease. Hospitalisation rates of children <5 years of age vary from 3.8/1,000/year in Denmark to 12.8 in Ireland. The proportion hospitalised as a ratio of those medically assessed varied from 1 in 17 in Ireland to 1 in 80 in Spain.

In Ireland, rotavirus became a notifiable disease in 2004. Since then there has been a consistent and sustained rise in notifications, most aged less than 4 years (see Figures 19.1 and 19.2). However, since almost all children are infected by their fifth birthday, there is very significant under-notification.

Figure 19.1. Number of cases of rotavirus and rate per 100,000 population 0-4 years by year, 2006 to 2015
(Source: HPSC)

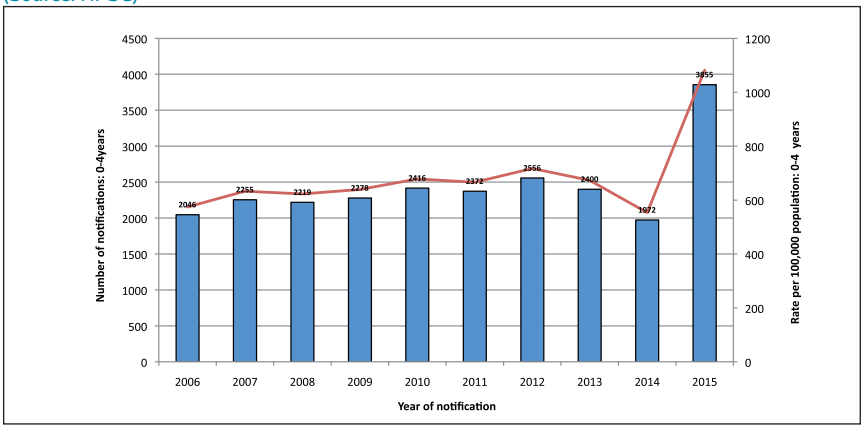
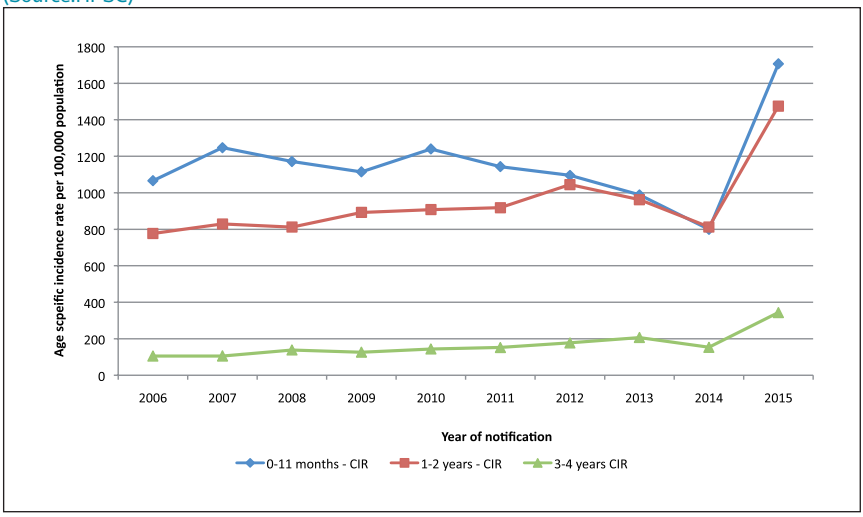


Figure 19.2. Figure 19.2. Age specific incidence rate per 100,000 population by age group 2006 - 2015
(Source:HPSC)



Effects of rotavirus

The virus damages the mature enterocytes of the small intestinal villi, where it produces an enterotoxin which causes epithelial necrosis, atrophy and desquamation. This results in reduced absorption of carbohydrates, salt and water, and in secretory and osmotic diarrhoea.

Virus shedding in symptomatic cases parallels the temporal development of illness. Virus can be detected in faeces coincident with or slightly before the onset of symptoms and in the majority for up to 8 days after onset. More severe diarrhoea may be associated with shedding of the virus in stools for up to 30 days. Asymptomatic excretion of rotaviruses in stool has been described in children and adults, and may play a role in transmission, particularly in nosocomial settings.

There is a wide spectrum of symptoms, ranging from none through mild diarrhoea to severe gastroenteritis with dehydration, electrolyte imbalance and shock. The stools are generally watery and yellow, without mucous or blood. Vomiting usually lasts <48 hours, but may persist for 8-10 days. Other gastrointestinal symptoms generally resolve in 3-7 days. Occasionally diarrhoea may last for up to 3 weeks.

Up to one third of children have a temperature of >39^{0}C. Respiratory symptoms are present in 30 to 50 percent of cases. Rarely, encephalitis and meningitis may occur. Severe illness is more likely in those aged 4-24 months.

Hospitalisation for rotavirus gastroenteritis is associated with low birth weight (a likely proxy for prematurity), daycare attendance, another child aged <2 years in the household and maternal smoking. Breast feeding protects against hospitalisation.

Those who are immunocompromised, particularly those with T-cell immunodeficiencies or severe combined immune deficiency (SCID), and after bone marrow transplantation, may experience severe or prolonged gastroenteritis. Rotavirus does not appear to be a common cause of severe or persistent diarrhoea in individuals with HIV infection.

Diagnosis
The most widely used diagnostic laboratory method is antigen detection of virus in the stool. Strains may be further characterised by enzyme immunoassay or PCR, but this is not commonly done.

Rotavirus vaccines

Two vaccines are currently available. Efficacy for both vaccines has been demonstrated against gastroenteritis due to the most common rotavirus genotypes Both vaccines give up to 95% (C.I. 88-100%) protection against severe RV disease and over 70% protection against any RV disease.

In countries with a rotavirus vaccine programme, rotavirus disease and hospitalisations have been reduced by over 90%.

Rotarix (RV1) is a live monovalent attenuated human type G1P1A[8] virus vaccine. It is supplied as 1.5 ml of oral suspension in a pre-filled oral applicator.
Rotateq (RV5) is a live pentavalent reassortant human-bovine virus vaccine, containing five reassortant strains developed from human and bovine strains. It is supplied as a 2 ml solution in a pre-filled squeezable tube.

A list of the vaccines currently available can be found at www.hpra.ie

Both vaccines should be stored between +2°C to +8°C.

Dose and route of administration

1. **Rotarix (RV1)**.**Two** oral doses of 1.5 ml at 2 and 4 months of age. No restrictions are placed on the infant's feeding in relation to rotavirus vaccine.
2. **Rotateq (RV5)**. **Three** oral doses of 2ml, at 2, 4 and 6 months of age. No restrictions are placed on the infant's feeding in relation to rotavirus vaccine.

To reduce the likelihood of significant regurgitation

- the vaccine should be given at the beginning of the visit, while the infant is still happy, and before administering injections. As the vaccine contains sucrose it will help reduce the pain of the injections.
- the dropper containing the vaccine should be aimed down one side and toward the back of the infant's mouth. The dropper should not be inserted so far back that the infant gags.

In the unlikely event that an infant spits out or regurgitates most of the vaccine dose during the clinic visit, a single replacement dose should be given at the same vaccination visit.

Age and interval restrictions for administration

The minimum age for dose 1 of rotavirus vaccine is 6 weeks.
The minimum interval between doses is 4 weeks.
All doses must be given before 8 months 0 days, because of a lack of safety and efficacy data in older children.

Infants should ideally receive their first dose of Rotataq® before 13 weeks of age and Rotarix® vaccine before 16 weeks of age. If an infant is late presenting for vaccination, they can receive their first dose before the age of 6 months and 0 days (for Rotateq®) and 7 months and 0 days (for Rotarix®). The final dose can then be given before 8 months and 0 days.

All doses of rotavirus vaccine must be completed by 8 months and 0 days

Infants who get rotavirus gastroenteritis before receiving the full series of rotavirus vaccination should still be immunised, because the initial rotavirus infection might provide only partial protection against subsequent rotavirus disease.

Indications
Rotavirus vaccine is recommended for infants aged between 6 and 32 weeks for the prevention of rotavirus gastroenteritis.

Preterm Infants (<37 weeks gestation) (see Chapter 2)
Preterm infants are at increased risk for hospitalisation from rotavirus gastroenteritis during the first two years of life. In clinical trials, rotavirus vaccine was generally well tolerated in preterm infants, although relatively small numbers were evaluated. The benefits of rotavirus vaccination of preterm infants outweigh the risks of adverse events.

≤ 28 weeks gestation
Preterm infants born ≤ 28 weeks of gestation who are vaccinated while in hospital should have respiratory monitoring for 48-72 hours when given their first immunisations, particularly those with a previous history of respiratory immaturity.

If the infant has apnoea, bradycardia or desaturations after the first routine immunisation, the second immunisation should also be given in hospital, with respiratory monitoring for 48-72 hours. If the infant has been discharged no respiratory monitoring is necessary.

Infants vaccinated whilst in hospital do not need to be isolated from other infants. As the the live attenuated vaccine virus can be excreted from the infant for at least 14 days, standard infection control precautions should be followed to reduce the risk of transmission, until the vaccinated infant has been discharged.

Simultaneous Administration with other vaccines
Rotavirus vaccine can be administered before, along with or after all routinely recommended vaccines, any blood product and tuberculin.

As both licensed rotavirus vaccines contain approximately 20% sucrose they should be administered just before recommended injections instead of a sucrose solution, to reduce pain.

Interchangeability of rotavirus vaccines
Whenever possible the same rotavirus vaccine should be used to complete the series. However, if the brand is not available or is unknown, complete the series with the vaccine available, unless there is a contraindication. If any dose in the series was RV5 or the vaccine product is unknown for any dose in the series, a total of 3 doses of RV5 vaccine should be administered if the infant is at an age when the vaccine can still be given.

Contraindications
1. Anaphylaxis to the vaccine or syringe constituents.
2. Uncorrected congenital GIT malformation (e.g., Meckel's diverticulum) which would predispose an infant to intussusception.
3. Previous intussusception (see Adverse reactions below).
4. Severe combined immunodeficiency (SCID).
5. Hereditary fructose intolerance, sucrose-isomaltase deficiency or glucose-galactose malabsorption.

Precautions
1. Acute severe febrile illness – defer until recovery.
2. Moderate or severe vomiting or diarrhoea – defer until recovery. However, infants with mild acute gastroenteritis can be vaccinated, particularly if the delay in vaccination might make the infant ineligible to receive the vaccine, even though the immunogenicity and efficacy of the vaccine could be reduced.
3. Immunodeficiency (other than SCID). Little safety or efficacy data are available following administration of rotavirus vaccine to other infants who are immunocompromised or potentially immunocompromised. Thus, although vaccine strains of rotavirus are considerably attenuated their administration to infants with known or suspected immunodeficiency other than SCID should be based on careful consideration of potential benefits and risks. HIV positive infants and those of unknown HIV status should receive rotavirus vaccine.

4. Contacts of immunocompromised persons. The vaccine virus could be transmitted from the infant to severely immunocompromised contacts through faecal material for at least 14 days. However, vaccination of the infant will offer protection to household contacts from wild-type rotavirus disease and outweigh any risk from transmission of vaccine virus to any immunocompromised close contacts.

   All members of the household should employ measures such as good handwashing and correct disposal of nappies after changing a nappy or otherwise coming in to contact with the faeces of a vaccinated child.

Adverse reactions

Local: Generally rotavirus vaccines are very well tolerated. Loss of appetite, diarrhoea or vomiting may occur, but are no more common than when compared with placebo.

General: Irritability, rash and pyrexia may occur but are no more common than when compared with placebo.

Post-marketing surveillance of both rotavirus vaccines has detected a small increased risk of intussusception (about 1-2/100,000 infants vaccinated) within 7 days of administration.

The benefits of rotavirus vaccination far exceed the risk of intussusception. As a precaution, healthcare professionals should advise parents/guardians promptly to report symptoms suggestive of intussusception (spasmodic abdominal pain, vomiting, bloody diarrhoea).

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