Rotavirus

Factsheet for healthcare practitioners

Background

In July 2013 a new vaccine was introduced into the childhood immunisation schedule.[1] This vaccine offers infants protection against the most common strains of rotavirus. Rotavirus is the most common cause of gastroenteritis among children and results in a significant number of young children being admitted to hospital each year. The vaccine used for this programme is called Rotarix®.

In 2009, the JCVI (Joint Committee on Vaccination and Immunisation) considered the evidence on
a) the burden of rotavirus infection and
b) the cost-effectiveness of rotavirus immunisation.

Based on the available evidence, the JCVI advised that the licensed rotavirus vaccines would have a significant impact on reducing gastroenteritis in young children and that the UK health departments should introduce the vaccines if they could be procured at a cost-effective price.[2] This advice was reiterated in 2011 following consideration of a further cost-effectiveness study.

In November 2012, the vaccine was procured at a price that meant the programme would be cost-effective. The programme started on 1 July 2013.[1]

Rotavirus

What is rotavirus?

Rotavirus is a highly infectious virus that causes gastroenteritis and is the most common cause of gastroenteritis among young children. Infections are often recurrent. Most children will experience at least one rotavirus infection by five years of age.

Rotavirus infection causes gastroenteritis that usually lasts from three to eight days.

Gastroenteritis can cause dehydration, which can be very serious, especially in young infants, requiring hospitalisation for intravenous rehydration.

Rotavirus is highly infectious and spreads mainly via the faecal-oral route.

Who is affected by rotavirus?

Rotavirus can affect people of all ages but the highest incidence is in young children. It is estimated that rotavirus infections cause around half of all gastroenteritis in children under five years of age.

As mentioned previously, young infants are also more likely to suffer from dehydration if they become infected with rotavirus than older children or adults.

The rotavirus vaccination programme

The rotavirus vaccination programme was introduced in all parts of the UK in July 2013.

Rotavirus vaccination is also part of the routine infant immunisation programme in a number of other countries including Australia, Canada and the USA. In the USA, studies have shown that rotavirus-related hospital admissions for young children have been cut by more than two thirds since rotavirus vaccination was introduced.[3]

Does the vaccine protect against all causes of gastroenteritis in young children?

The Rotarix® vaccine protects against the most common strains of rotavirus. It doesn't protect against other types of virus (eg norovirus) or bacteria (eg *Salmonella*) that can cause gastroenteritis. However, as rotavirus is the most common cause of gastroenteritis in young infants, it will have a significant impact on the total number of young children who become ill with gastroenteritis and the number with severe disease.

How many doses will infants receive?

The objective of the programme is to provide two doses of Rotarix® to infants before 24 weeks of age (ie 23 weeks and six days).[4] Infants will be offered two doses with an interval of at least four weeks between doses: at eight weeks (two months) and again at 12 weeks (three months). It is preferable that the full course of two doses of Rotarix be completed before 15 weeks (ie 14 weeks and six days of age), but it must be completed by 24 weeks (ie 23 weeks and six days).

When will infants receive the vaccine?

- All children scheduled to receive their primary vaccines at age eight weeks and 12 weeks should be offered the rotavirus vaccine, that is, **two doses**, four weeks apart. Both doses should be given by 24 weeks of age (ie 23 weeks and six days).

- Infants who have received their first dose of vaccine by week 15 (ie 14 weeks and six days) can receive their second dose of Rotarix® as long as it is given by week 24 (ie 23 weeks and six days).

- Infants who have not received their first dose by week 15 (ie 14 weeks and six days) should not be offered Rotarix®.

- Infants may receive their first dose of primary immunisations from six weeks of age in exceptional circumstances, eg pre-travel, but it is not routinely recommended to offer infants vaccine before two months of age. Rotarix® is licensed from six weeks of age.

What if the infant does not receive the first dose at age two months?

If the infant presents before they are 15 weeks of age (ie 14 weeks and six days), they should be offered their first dose. The second dose should be given at least four weeks later and must be given before 24 weeks of age (ie 23 weeks and six days).

Infants who present for their first dose after 15 weeks of age (ie 14 weeks and six days) should not be offered Rotarix®.

What if it is more than four weeks since the first dose?

If the course is interrupted, it should be resumed but not repeated. If the infant is still less than 24 weeks of age (ie 23 weeks and six days), the second dose should be given. If they are aged 24 weeks or older, the second dose must not be given.

Why can't the first dose of vaccine be given to children over 15 weeks?

Vaccination should not be initiated for infants over 15 weeks of age (ie 14 weeks and six days) because of insufficient data on the safety of a first dose of rotavirus vaccine in older infants. Both doses should be given by 24 weeks of age (ie 23 weeks and six days)

The vaccine

What vaccine is given?

The vaccine that is used is Rotarix®. It is a live attenuated vaccine (a weakened form of virus that cannot cause disease in the infant but which protects against rotavirus).

This is an **oral** vaccine, which must **not** be injected.

How should the Rotarix® vaccine be stored?

Rotarix® must be stored in accordance with the manufacturer's instructions. As with most vaccines, Rotarix® should be stored in a refrigerator between +2°C and +8°C.

The vaccine should be stored in the original packaging. This makes it easy to identify in the vaccine refrigerator and will protect it from light.

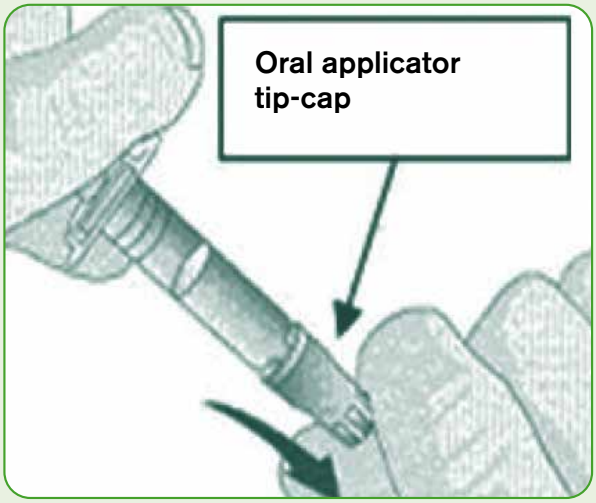
How is the vaccine presented?

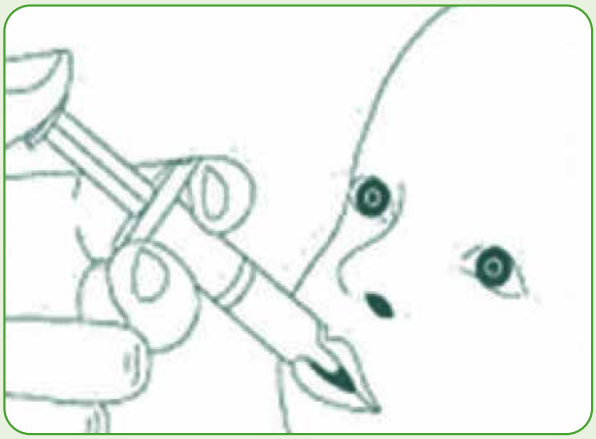
- The vaccine is presented as a pre-filled oral applicator containing 1.5ml oral suspension.
- It is ready to use (no reconstitution or dilution is required).
- It is a clear, colourless liquid, free of visible particles.
- It should be visually inspected for any foreign particulate matter and/or physical appearance. In the event of either being observed, discard the vaccine.

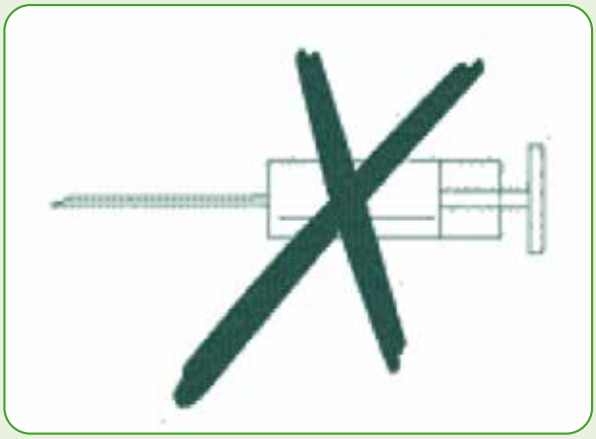
How is the vaccine given?

- Give the oral Rotarix® vaccine at the beginning of the visit, before administration of any intramuscular vaccines.
- The infant should be seated in a reclining position. Remove the protective tip from the oral applicator.

- Administer orally (ie into the child's mouth, towards the inner cheek) the entire contents of the oral applicator.
- The vaccine must not be injected.







Images cortesy of GSK[5]

What happens if the baby spits the vaccine out?

If the infant spits out or regurgitates most of the vaccine, a single replacement dose may be given at the same visit.

Can the baby be fed before or after receiving the vaccine?

Yes, there are no restrictions on the infant's feeding before or after immunisation.

Can Rotarix® be given at the same time as other vaccines?

Yes, Rotarix® can be given at the same time as the other vaccines administered as part of the routine childhood immunisation programme and should ideally be given at the scheduled two month and three month immunisation visits.[6]

Rotarix® can also be given at the same time as BCG or at any time before or after it.

As discussed previously, it is suggested that Rotarix® is given at the beginning of the visit before administration of intramuscular vaccines, which may unsettle the infant.

As Rotarix® is a live vaccine, can it be passed onto others?

There is a potential for transmission of the live attenuated virus in Rotarix® from the infant to severely immunocompromised contacts through faecal material for at least 14 days.[5,7] However, vaccination of the infant will offer protection to household contacts from wild-type rotavirus disease and outweighs any risk from transmission of vaccine virus to any immunocompromised close contacts.

Those in close contact with recently immunised infants should, as always, observe good personal hygiene, eg washing their hands after changing a child's nappy.

Are there any infants who can't have Rotarix®?

There are very few infants who cannot receive Rotarix®. Where there is any doubt, appropriate advice should be sought on the circumstances under which the vaccine could be given from appropriate registered healthcare practitioners, eg child's paediatrician, immunisation coordinator or the Public Health Agency Duty Room (0300 555 0119).

Rotarix® should **not** be given to:

- infants with a confirmed anaphylactic reaction to a previous dose of rotavirus vaccine;
- infants with a confirmed anaphylactic reaction to any components of the vaccine;

- infants with a previous history of intussusception;
- infants aged 24 weeks or over (ie beyond 23 weeks and six days);
- infants presenting for the first dose of vaccine over 15 weeks of age;
- infants with severe combined immunodeficiency (SCID) disorder;
- infants who have a malformation of the gastrointestinal tract that could predispose them to intussusception;
- infants with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltose insufficiency.

Administration of rotavirus vaccine **should be postponed** in infants:

- suffering from acute severe febrile illness. This is to avoid confusing the diagnosis of any acute illness by wrongly attributing any signs and symptoms to adverse effects of the vaccine;
- suffering from acute diarrhoea or vomiting. This is to ensure that the vaccine is not regurgitated or passed through the intestines too quickly, which could reduce the effectiveness of the vaccine.

Can the vaccine be given to children who are immunocompromised?

Rotavirus vaccine should not be administered to infants known to have SCID. Although the vaccine is a live attenuated virus, with the exception of SCID, the benefit from vaccination may exceed any risk in other forms of immunosuppression. Therefore, there are very few infants who cannot receive rotavirus vaccine. Where there is doubt, appropriate advice should be sought from the child's paediatrician, an immunisation coordinator or the Public Health Agency Duty Room rather than withholding vaccination.

From clinical trials with HIV-infected infants, the safety profile was similar between Rotarix® and placebo recipients.[7] Therefore, vaccination is advised in HIV-infected infants. Additionally, infants with unknown HIV status but born to HIV positive mothers should be offered vaccination.[4]

Can premature infants receive the vaccine?

It is important that premature infants have their immunisations at the appropriate chronological age, according to the schedule. As with other vaccinations, the occurrence of apnoea following vaccination is especially increased in infants who were born very prematurely.

Very premature infants (born ≤ 28 weeks of gestation) who are 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 child 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.

Given the benefit of vaccination in this group of infants, vaccination should not be withheld or delayed.

Should rotavirus vaccine be offered to hospitalised infants?

Infants, including those that are born prematurely should be offered rotavirus vaccine at their chronological age, if the infant is clinically stable. Hospitalised pre-term infants are particularly vulnerable to rotavirus infection and its complications and should be vaccinated as per recommendations. Delaying vaccination until discharge from hospital places the infant at a risk of acquiring the infection or receiving the vaccination too late and at a time where the risk of intussusception is greatest. Rotarix® is a highly attenuated vaccine virus with a very low risk of clinical disease even in vulnerable infants. Infants vaccinated whilst in hospital do not need to be isolated from other infants as basic standard precautions should be followed to reduce the risk of transmission of the vaccine virus to others.

If the child has already had rotavirus infection, can they still receive the vaccine?

If a child has had confirmed or suspected natural rotavirus infection, they should still receive the Rotarix® vaccine as scheduled to provide protection against future infection.

If the child is suffering from acute diarrhoea or vomiting, the administration of the rotavirus vaccine should be postponed. This is to make sure that the vaccine is not regurgitated or passed through the intestines too quickly, which could reduce the effectiveness of the vaccine.

Does Rotarix® contain thiomersal?

No, there is no thiomersal or any other preservatives in Rotarix®

Does Rotarix® contain latex?

The plunger stopper and protective tip cap are both rubber butyl, which should not affect latex sensitive individuals.

What are the potential side effects of this vaccine?

The most common adverse events observed following the administration of Rotarix® are:

- diarrhoea;
- irritability.

Other reactions commonly reported are:

- vomiting;
- abdominal pain;
- flatulence;
- skin inflammation;
- regurgitation of food;
- fever;
- loss of appetite.

The full list of adverse reactions associated with Rotarix® is available in the marketing authorisation holder's Summary of Product Characteristics.[5]

Anaphylaxis

As with all vaccines, there is a very rare possibility of a severe allergic reaction called anaphylaxis. All registered healthcare practitioners responsible for immunisation should be trained to recognise and treat anaphylaxis.

Parents/guardians should be advised to seek medical advice if there is any severe adverse event including severe vomiting and diarrhoea with a fever.

Is there a link between rotavirus vaccine and intussusception?

Research from some countries suggests that Rotarix® may be associated with a very small increased risk of intussusception within seven days of vaccination, possibly two cases per 100,000 first doses given, and the Rotarix® prescribing information includes this as a possible side effect. The benefits of vaccination in preventing the consequences of rotavirus infection outweigh the small potential risk in young infants.[4]

Because of the potential risk, and to reduce the likelihood of a temporal association with rotavirus vaccine, the first dose of vaccine should not be given after 15 weeks of age.

Parents/guardians should be advised to contact their doctor immediately if their infant develops severe vomiting or abdominal pain and passes what looks like red currant jelly in their stools.

What is intussusception?

Intussusception is a naturally-occurring condition of the intestines with a background annual incidence of around 120 cases per 100,000 children aged under one year. Intussusception occurs when a section of the bowel folds in on itself like a telescope closing. When this occurs, it creates a blockage in the bowel.

The main symptom of intussusception is severe abdominal pain that comes and goes. Each episode tends to last two to three minutes and, in between episodes, the infant will look very pale, tired and floppy. After 12 hours or so, the pain becomes more constant and the infant will usually go off food and may vomit. Due to vomiting, the infant may become dehydrated.[2]

Intussusception can be life-threatening and requires prompt medical treatment.

Is it alright for babies who have recently received rotavirus vaccine to be taken swimming?

There is no reason for recently vaccinated babies not to be taken swimming since the vaccine virus is highly attenuated and it should also be killed by chlorine.

Can rotavirus vaccine be given via a feeding tube if a baby has one in situ?

Given the very small volume of fluid in a dose of rotavirus vaccine, children with feeding tubes should preferably be given the vaccine orally, unless absolutely necessary to give it via the tube.

Can infants who have recently received an antibody-containing blood product (eg blood transfusion or HBIG) still receive live rotavirus vaccine?

Rotavirus vaccine may be administered at any time before, at the same time as, or after administration of any blood product, including antibody-containing

products, following the routinely recommended immunisation schedule for infants who are eligible for vaccination. There are no data currently available as to whether the immune response to rotavirus vaccine in infants is affected by blood products.[8] However, as infants receive two doses of rotavirus vaccine, they have two opportunities to make a good antibody response to the vaccine.

Can rotavirus vaccine be given to infants who are receiving anti-reflux medications including antacids?

The rotavirus vaccine itself actually contains antacid (calcium carbonate) in the diluent to protect the virus during its passage through the stomach and prevent its inactivation due to the acidic environment.[9] Reflux medicines should therefore not affect the immune response to the vaccine and infants taking these medications should receive the vaccine as scheduled.

If the first dose of rotavirus vaccine is inadvertently given to a child age 15 weeks 0 days or older, what advice should be given and should the child still receive a second dose four weeks later?

Children who inadvertently receive the first dose of rotavirus vaccine at age 15 weeks or older should still receive their second dose four weeks later (providing that they will still be under 24 weeks of age at this time). The reason for the 15 week age limit is not only to provide protection before the main burden of disease but also to avoid a temporal association with intussusception.

Intussusception is a naturally-occurring condition where part of the intestine prolapses, or telescopes, into another part causing an obstruction. The background risk of intussusception in the UK increases rapidly after three months to peak at around five months of age. Research from some countries suggests that rotavirus vaccine may be associated with a very small increased risk of intussusception within seven days of vaccination (possibly two cases per 100,000 first doses given). Although there is no clear evidence that the risk of intussusception increases if the first dose of rotavirus vaccine is given later than 15 weeks, it will be more difficult to ascertain, if the child develops intussusception, whether this was due to the vaccine or was naturally occurring. No specific clinical action needs to be taken if the vaccine is inadvertently given after 15 weeks of age but, as with all parents of children receiving rotavirus vaccination, the parents should be aware of the symptoms of intussusception. A risk review should also be carried out to ascertain why the vaccine was given outside the national recommendations and steps taken to ensure it doesn't happen again.

Similarly, if a child inadvertently receives rotavirus vaccine over 24 weeks of age, no specific clinical action needs to be taken but immunisers should be reminded that rotavirus vaccine should not be given to infants older than 24 weeks, even if they haven't completed the two dose schedule.

Where can I get more information?

The Green Book rotavirus chapter
www.gov.uk/government/publications/rotavirus-the-green-book-chapter-27b

Health professional resources
www.publichealth.hscni.net/directorates/public-health/health-protection/vaccine-preventable-diseases-and-immunisation-0

Marketing authorisation holder's Summary of Product Characteristics
www.medicines.org.uk/emc/product/2739/smpc

Medicines and Healthcare products Regulatory Agency (MHRA) – for reporting adverse reactions.
www.mhra.gov.uk

More information on the clinical presentation of rotavirus from NHS Choices
www.nhs.uk/conditions/Rotavirus-gastroenteritis/Pages/Introduction.aspx

References to original source materials:

1. Introduction of rotavirus vaccine for babies aged 2 and 3 months from 1 July 2013 into the routine childhood vaccination programme www.dhsspsni.gov.uk/hss-md-11-2013.pdf

2. JCVI statement on Rotavirus 2009 http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/document s/digitalasset/dh_095177.pdf

3. Tate JE, Cortese MM, Payne DC, Curns AT, Yen C, Esposito DH, Cortes JE, Lopman BA, Gentsch JR, Parachar UD (2011) Uptake, impact, and effectiveness of rotavirus vaccination in the United States: review of the first 3 years of postlicencsure data. *Pediatr Infect Dis J* 30 (1 Suppl) S56-60

4. Rotavirus Green Book Chapter https://www.gov.uk/government/organisations/public-health-england/series/immunisation-against-infectious-disease-the-green-book

5. Rotarix SPC, available on ema website http://www.medicines.org.uk/emc/medicine/17840/SPC/Rotarix

6. Anderson EJ. (2008) Rotavirus vaccines: viral shedding and risk of transmission. *Lancet Infect Dis* 8 (10) 642-9

7. Steele AD, Madhi SA, Louw CE, et al (2011) Safety, Reactogenicity, and Immunogenicity of human rotavirus vaccine RIX4414 in Human Immunodeficiency Virus positive infants in South Africa. *Pediatr Infect Dis J* 30 (2) 125-30

8. MMWR Prevention of Rotavirus Gastroenteritis Among Infants and Children Recommendations of the Advisory Committee on Immunization Practices (ACIP) February 6, 2009 / 58(RR02);1-25 (available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5802a1.htm?s_cid=rr5802a1_e)

9. National Vaccine Information Center. Rotavirus and rotavirus vaccine. Available at www.nvic.org/vaccines-and-diseases/Rotavirus.aspx

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