WEEKLY EPIDEMIOLOGICAL REPORT

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231, de Saram Place, Colombo 01000, Sri Lanka
Tele: + 94 11 2695112, Fax: +94 11 2696583, E mail: epidunit@sltnet.lk
Epidemiologist: +94 11 2681548, E mail: chepid@sltnet.lk
Web: http://www.epid.gov.lk

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Rotavirus Gastro-Enteritis (Part II)

This is the second in a series of two articles on Rotavirus Gastro-Enteritis.

Rotavirus vaccines

Currently available vaccines are oral live attenuated rotavirus strains of human and/or animal origin that replicate in the human intestine. Two oral rotavirus vaccines are marketed internationally: the monovalent (RV1) and the pentavalent (RV5) vaccines.

Lanzhou lamb rotavirus vaccine, manufactured by the Lanzhou Institute of Biomedical Products in China and Rotavin-M1, manufactured by Polyvac in Viet Nam, are not available internationally and hence not further discussed here.

The monovalent human rotavirus vaccine (lyophilized and liquid) RV1 is a live, oral vaccine originating from a G1P[8] strain that was isolated from a case of infantile gastroenteritis. This strain has undergone multiple passages in tissue culture and the resulting attenuated vaccine strain, RIX4414, is propagated in Vero cells. First prepared as a lyophilized vaccine, a ready-to-use liquid formulation containing the same RIX4414 strain has subsequently been developed for 2 presentations: oral applicator and squeezable tube. The 2 vaccine doses are administered at an interval of at least 4 weeks. According to the manufacturer, the first dose should be administered to infants ≥6 weeks of age and the second dose prior to 24 weeks of age.

The pentavalent human-bovine reassortant rota virus vaccine RV5 is an oral vaccine that contains 5 reassortant rota viruses developed from human and bovine (WC3) parent rotavirus strains. Four WC3-based reassortants express one of the VP7 proteins G1, G2, G3 or G4 from the human strains and the VP4 protein P7[5] from the bovine strain, whereas the fifth reassortant virus expresses the VP4 protein P1A[8] from a human strain and the G6 protein from the bovine parent strain. The re-assortants are subsequently propagated in Vero cells using standard cell-culture techniques.

The manufacturer's recommended schedule prescribes 3 oral doses at ages 2, 4 and 6 months. The first dose should be administered between ages 6–12 weeks and subsequent doses at intervals of 4–10 weeks. The manfacturer recommends that all 3 doses should be ad ministered by age 32 weeks.

Efficacy and effectiveness of the rotavirus vaccine

A recent Cochrane review shows that RV1 and RV5 are most efficacious against severe RVGE in sub regions with very low or low child and adult mortality although the vaccines are also efficacious in sub-regions with high child mortality and high or very high adult mortality.

Based on 11 RCTs of RV1 and 6 RCTs of RV5, this Cochrane review showed protection against severe RVGE after 1 and/or 2 years of follow up, ranging from approximately 80%–90% with modest waning over the period of observation in countries with very low or low child and adult mortality as compared to approximately 40%–60% efficacy over 2 years of follow up in countries with high child mortality and high or very high adult mortality.

However, since the incidence of severe rotavirus disease is significantly higher in high child mortality settings, the numbers of severe disease cases and deaths averted by vaccines in these settings are likely to be higher than in low mortality settings, despite the lower vaccine efficacy.

Data from case-control studies show that RV1 and RV5 are more efficacious when the full course is given, but some protection may also be achieved following an incomplete vaccination series. For example, RV5 exhibits substantial effectiveness against RVGE before completion

Contents	Page

of the full 3 dose regimen. The ability to interchange RV1 and RV5 has not been studied.

RV1 and RV5 have similar efficacy against severe RVGE in countries where a high diversity of strains co-circulate, suggesting an important role for heterotypic protective immunity. However, indirect evidence suggest that homotypic immunity also plays a role in protection against subsequent RV infection. Characterization of RV strains present in the environment post-vaccination is needed to exclude population-based selection of 'escape' strains due to long-term pressure exerted by homotypic immunity.

simultaneous administration of RV1 or RV5 with other vaccines of the infant immunization programme, including combined diphtheria, tetanus toxoid and acellular pertussis vaccine (DTaP), inactivated poliovirus vaccine (IPV), H. influenza type b conjugate (Hib), hepatitis B vaccine, and pneumococcal conjugate vaccine have been shown not to interfere significantly with the protective immune responses or safety profile of the respective vaccines.

Although OPV may have an inhibitory effect on the immune response to the first dose of both rotavirus vaccines, this interference does not persist after administration of subsequent doses of rotavirus vaccines.

Breastfeeding and prematurity (<37 weeks' gestation) do not seem to significantly impair the response to the rotavirus vaccines

Contraindications for using rotavirus vaccines are severe hypersensitivity to any of their components and severe immunodeficiency including severe combined immunodeficiency (SCID). Vaccination should be postponed in case of ongoing acute gastroenteritis or fever with moderate to severe illness. These vaccines are not routinely recommended for infants with a history of intussusception or intestinal malformations possibly predisposing for intussusception.

In 2010, contamination of RV1 with full length DNA from porcine circovirus was reported and subsequently, low levels of DNA fragments of this virus were also detected in bulk lots of RV5. Porcine circovirus is not known to infect or cause disease in humans. The extensive clinical data supporting the safety of both RV1and RV5 and the benefits of rotavirus vaccination for children, the benefits of vaccination far outweigh any currently known risk associated with use of either rotavirus vaccine.

The risk of intussusception

Intussusception, an intestinal invagination resulting in obstruction, is characterized clinically by intermittent severe abdominal pain, blood in the stools, a palpable lump in the abdomen, and vomiting. This serious and potentially fatal condition was associated primarily with the first of the 3 oral vaccine doses and the highest attributable risk was found in infants >3 months of age. The pathogenic mechanisms involved in intussusception following rotavirus vaccination remain poorly defined.

Post-marketing surveillance showed that the previously marketed rotavirus vaccine, RotaShield® (Wyeth-Lederle), carried an attributable risk of intussusceptions estimated at 1:10 000 recipients.

RCTs conducted so far have lacked power to rule out very small relative risks of association between RV1or RV5 and intussusception in narrow risk windows, for example the 1–7 day period after dose 1. In some but not all settings, post-marketing surveillance of both currently available rotavirus vaccines has detected a small increased risk of intussusceptions (about 1–2/100 000 infants vaccinated) shortly after the first dose. Where present, this risk is 5–10 times lower than that observed with the previously licensed RotaShield®, and the benefits of rotavirus vaccination against severe diarrhoea and death from rotavirus infection far exceeds the risk of intussusception.

Administration of the first and last dose of RV1 and RV5 at different ages inside the recommended age window has not shown any impact on the incidence of serious adverse events including intussusception.

No data are available on the possible risk of such events outside the recommended age window. There is limited information on the background rates of intussusception in settings of high mortality due to RVGE and no data on the risk of intussusception following rotavirus vaccination in such settings

Optimizing immunization schedules

Ideally, vaccination schedules should be designed to provide benefits to those at highest risk of severe disease and death. Based on pooled data from studies of 38 populations, at least 3 of which are from each WHO Region, 1%, 3%, 6%, 8%, 10%, 22% and 32% of all RVGE events had occurred by age 6, 9, 13, 15 and 17, 26 and 32 weeks, respectively, although with substantial heterogeneity between populations. Mortality was limited to RVGE events before 32 weeks of age.

Although in many parts of the world there are relatively few admissions for RVGE before the scheduled first dose of the rotavirus vaccine (at the age 6–12 weeks), RVGE in very young children is more common in low income settings. Children in the poorest, typically rural, households with the highest risk of mortality seem to have the earliest exposure to rotavirus and the lowest level of vaccine protection.

To maximize its impact, the rotavirus vaccine has to be given before RVGE occurs and before a sizeable proportion of the target population acquires natural infection. The impact of rotavirus vaccination depends on effectiveness, timeliness and coverage. In developing countries where natural infection occurs early, completion of the immunization schedule early in infancy is desirable, though programmatically challenging.

Previously, WHO recommended that rotavirus immunization be initiated by 15 weeks of age when background intussusception rates are reportedly low. However, this policy could exclude a substantial number of children from vaccination, especially in low income countries where delays in vaccination are common.

A model was used to predict the number of deaths prevented by rotavirus vaccination and the number of intussusception deaths caused by rotavirus vaccination when administered on the previously recommended, restricted schedule (initiate by 15 weeks and complete by 32 weeks) versus a schedule allowing vaccination up to 3 years of age.

The model showed an increase in the number of deaths due to intussusception, while showing a higher number of lives saved by allowing vaccination up to 3 years of age in low and middle income countries. The additional lives saved by removing age restrictions for rotavirus vaccination would by far outnumber the excess vaccine-associated intussusception deaths.

Source-Rota Virus vaccine-available from *http://www.who.int/wer/2013/wer8805.pdf*

Compiled by Dr.Madhava Gunasekera of the Epidemiology Unit

Table 4: Selected notifiable diseases reported by Medical Officers of Health 14th Dec– 20th Dec(51th Week)

RDHS Division	Dengue Fever		Dysentery		Encephalitis		E Fever		F Poisoning		Leptospirosis		T Fever		V Hepatitis		H Rabies		Chickenpox		Meningitis		Leishmania-sis		WRCD %	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	T*	C**
Colombo	249	10359	4	231	0	18	3	172	0	59	1	215	1	10	1	89	0	1	2	457	0	73	0	1	**62**	**38**
Gampaha	23	3695	2	224	0	24	1	54	0	41	3	485	0	25	0	194	0	0	3	177	3	100	0	5	**53**	**47**
Kalutara	49	1852	3	197	0	21	0	83	0	27	5	447	0	6	0	29	0	0	4	291	3	88	0	0	**46**	**54**
Kandy	18	1731	6	173	0	13	0	31	0	24	2	94	0	103	2	133	0	0	2	162	1	26	0	5	**74**	**26**
Matale	4	472	1	115	0	4	0	25	1	11	0	68	0	4	0	60	0	0	1	49	0	39	0	13	**62**	**38**
NuwaraEliya	6	265	2	175	0	4	0	17	0	217	0	33	0	65	0	25	0	0	0	164	0	15	0	0	**69**	**31**
Galle	29	884	4	136	1	20	0	7	0	89	14	255	0	67	0	17	0	2	4	338	1	48	0	3	**79**	**21**
Hambantota	6	337	4	72	0	3	0	16	0	38	1	181	4	71	0	94	0	0	0	101	2	57	11	360	**75**	**25**
Matara	10	480	1	99	0	17	0	30	0	30	3	175	2	97	4	157	0	2	3	266	3	93	1	104	**100**	**0**
Jaffna	19	755	10	470	0	13	8	342	0	114	1	10	25	404	0	17	0	2	0	153	1	59	0	0	**83**	**17**
Kilinochchi	1	65	0	57	0	0	0	16	0	5	0	9	0	17	0	0	0	2	1	3	0	7	0	14	**50**	**50**
Mannar	0	69	3	79	0	3	0	71	1	36	0	15	0	22	0	2	0	0	0	12	0	7	0	4	**80**	**20**
Vavuniya	3	90	2	80	0	14	1	15	0	32	0	51	0	3	0	4	0	2	0	23	2	38	0	16	**75**	**25**
Mullaitivu	0	122	1	33	0	3	0	11	0	47	0	38	0	7	0	2	0	2	0	8	0	7	0	15	**20**	**80**
Batticaloa	9	554	9	398	0	5	0	11	0	74	2	44	0	2	1	17	0	3	1	48	1	9	0	0	**79**	**21**
Ampara	5	212	2	204	0	1	0	5	0	12	2	42	0	1	0	11	0	0	2	106	1	21	0	3	**57**	**43**
Trincomalee	1	196	0	74	0	3	1	7	0	4	0	61	0	15	0	4	0	1	0	41	0	5	0	30	**42**	**58**
Kurunegala	15	2725	2	229	0	43	0	43	0	31	2	387	0	52	0	66	0	1	8	381	0	105	1	61	**74**	**26**
Puttalam	10	904	2	83	0	7	0	18	0	36	2	46	1	15	0	7	0	2	1	89	0	36	0	12	**46**	**54**
Anuradhapura	11	544	9	122	0	17	0	3	0	71	5	335	1	28	0	30	0	2	2	177	2	108	6	430	**63**	**37**
Polonnaruwa	11	494	3	101	0	3	0	14	0	73	1	183	0	3	0	36	0	2	4	152	1	25	2	176	**57**	**43**
Badulla	5	523	3	215	0	5	0	22	0	12	1	62	0	95	0	47	0	1	4	141	1	74	1	8	**53**	**47**
Monaragala	0	264	2	129	0	7	0	26	0	38	1	207	0	69	2	195	0	2	4	70	0	28	0	14	**45**	**55**
Ratnapura	8	1705	1	395	0	84	1	44	0	21	4	411	0	77	9	607	0	1	3	207	1	92	0	18	**67**	**33**
Kegalle	22	1207	5	148	0	17	1	37	0	11	4	307	2	76	2	254	0	0	5	357	2	115	0	2	**91**	**9**
Kalmune	0	503	1	195	0	3	0	6	0	130	0	11	0	3	0	5	0	0	0	107	0	13	0	1	**31**	**69**
SRI LANKA	**514**	**31007**	**82**	**4434**	**1**	**352**	**16**	**1126**	**02**	**1283**	**54**	**4172**	**36**	**1337**	**21**	**2102**	**0**	**28**	**54**	**4080**	**25**	**1288**	**22**	**1295**	**65**	**35**

Source: Weekly Returns of Communicable Diseases (WRCD).

*T=Timeliness refers to returns received on or before 14th December , 2013 Total number of reporting units 337. Number of reporting units data provided for the current week:219C** -Completeness

A = Cases reported during the current week. B = Cumulative cases for the year.H Rabies*= Human Rabies, E Fever*=Enteric Fever, F Poison* =Food Poisoning, T Fever*=Typhus Fever, V Hepatitis*=Viral Hepatitis

Table 1: Vaccine-Preventable Diseases & AFP 14th Dec – 20th Dec2013 (51th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2013	Number of cases during same week in 2012	Total number of cases to date in 2013	Total number of cases to date in 2012	Difference between the number of cases to date in 2013 & 2012
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	01	01	01	00	00	00	00	00	00	03	01	105	74	+ 41.9%
Diphtheria	00	00	00	00	00	00	00	00	00	00	-	00	-	-
Mumps	00	00	04	01	04	01	00	00	03	13	17	1469	4255	-65.5 %
Measles	10	04	12	00	01	03	05	02	08	45	03	3955	77	+5036.4%
Rubella	00	00	00	00	00	00	00	00	00	00	-	27	-	-
CRS**	00	00	00	00	00	00	00	00	00	-	-	-	-	-
Tetanus	00	00	00	00	00	00	00	00	00	00	00	24	13	+ 84.6%
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	-	-	-	-	-
Japanese Encephalitis	01	00	01	00	00	00	00	00	00	00	00	68	101	-32.7%
Whooping Cough	00	00	00	00	00	00	00	00	00	00	00	85	101	- 15.8%
Tuberculosis	33	194	19	13	11	17	17	04	17	325	224	8691	8594	+1.2%

Key to Table 1 & 2

Provinces: W: Western, C: Central, S: Southern, N: North, E: East, NC: North Central, NW: North Western, U: Uva, Sab: Sabaragamuwa.

RDHS Divisions: CB: Colombo, GM: Gampaha, KL: Kalutara, KD: Kandy, ML: Matale, NE: Nuwara Eliya, GL: Galle, HB: Hambantota, MT: Matara, JF: Jaffna, KN: Killinochchi, MN: Mannar, VA: Vavuniya, MU: Mullaitivu, BT: Batticaloa, AM: Ampara, TR: Trincomalee, KM: Kalmunai, KR: Kurunegala, PU: Puttalam, AP: Anuradhapura, PO: Polonnaruwa, BD: Badulla, MO: Moneragala, RP: Ratnapura, KG: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS** =Congenital Rubella Syndrome

AFP and all clinically confirmed Vaccine Preventable Diseases except Tuberculosis and Mumps should be investigated by the MOH

Dengue Prevention and Control Health Messages

Thoroughly clean the water collecting tanks bird baths, vases and other utensils once a week to prevent dengue mosquito breeding.

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Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to chepid@sltnet.lk. **Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

ON STATE SERVICE

Dr. P. PALIHAWADANA
CHIEF EPIDEMIOLOGIST
EPIDEMIOLOGY UNIT
231, DE SARAM PLACE
COLOMBO 10