WEEKLY EPIDEMIOLOGICAL REPORT

A publication of the Epidemiological Unit,

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Vaccines against Japanese Encephalitis

It was decided to make all efforts to introduce live attenuated JE vaccine [LJEV] to the National EPI schedule at the earliest replacing the currently used killed JE vaccine. This decision was taken, at the National immunization Summit held in Colombo in January 2007 with the participation of all stakeholders of the programme .

With a view to implementing this decision currently with the support from PATH, the Epidemiology Unit has initiated a clinical trial in the Colombo district to ascertain the safety and immunogenicity of LJEV. Based on the preliminary results, the Advisory Committee on Communicable Diseases has at its last meeting in March 2008 decided to introduce live JE vaccine in place of the inactivated vaccine.

Type of JE vaccines

Three types of JE vaccines are currently in use in several JE endemic countries of the Asia-Pacific Region. They are namely:

(1) Mouse brain-derived inactivated vaccine;
(2) Cell culture-derived inactivated vaccine.
(3) Cell culture-derived live attenuated vaccine

Mouse brain-derived inactivated vaccine

The mouse brain-derived inactivated JE vaccine is produced in several Asian countries. Until recently, this has been the only type of JE vaccine commercially available in the international market. The commercially available mouse brain-derived JE vaccine is based either on the Nakayama strain, which was isolated in Japan in 1935, or on the Beijing-1 strain. Currently the mouse brain-derived vaccine is used in China, India, Sri Lanka and Thailand.

The mouse brain-derived JE vaccine [Beijing strain used in the public sector]is given subcutaneously in doses of 0.25 ml or 0.5 ml, the lower dose being for children aged 1-3years. Due to likely interference with remaining maternal antibodies, children are usually not vaccinated before the age of 1 year. The manufacturers of the internationally marketed vaccine recommend that primary childhood immunization involve 2 injections at an interval of 1-2 weeks. In several Asian trials, primary immunization has had a disease-preventing efficacy of > 95%; 91% efficacy was achieved in a placebo-controlled trial. There is no reduction of seroconversion rates when other childhood vaccines are given simultaneously. However, the primary vaccination schedules vary considerably among different Asian countries.

Cell culture-derived inactivated vaccine

This vaccine is manufactured in China and based upon the Beijing P-3 strain of JE virus. Primary immunization of infants with this formalin-inactivated vaccine results in about 85% protection. The vaccine is inexpensive, and 90 million doses are distributed for internal use in China every year. However, in China this vaccine will be gradually replaced by the cell culture-derived live attenuated vaccine.

Cell culture-derived live attenuated vaccine :

This Chinese vaccine is based on a stable neuro-attenuated strain of the JE virus (SA-14-14-2). In non-endemic areas, 1 single dose of this

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vaccine induced an antibody response in 83%-100% of children aged 6-7 years, and in older children when immunized twice at intervals of 1-3 months, 94%-100% showed a serological response. Side-effects are reported to be minimal. Although at least two doses are recommended, there is evidence that even a single dose can stimulate adequate immune response in the recipient of the vaccine as demonstrated more recently in Nepal.

Apart from hundreds of millions of doses used in China, India began introduction of this vaccine in eleven high endemic districts in five states.

The live attenuated SA 14-14-2 vaccine is recommended to be given as a single dose to children older than 8 months of age followed with a second opportunity at 2 years of age. However, the WHO recommendation at present is to give the vaccine to children above one year of age. The age of the first dose should be based on local age distribution of cases and the immunization schedule. The live JE vaccine has no additional contraindications to other live vaccines.

The SA 14-14-2 vaccine virus is a JE viral strain that has shown effectiveness in vitro against the P3; Nakayama; 12 Chinese JE field isolates; and JE strains from Thailand, Nepal, Vietnam, Indonesia, India, Japan, and the Philippines. This vaccine has been licensed in China for 18 years, and over 200 million doses have been given without any recorded significant adverse event. The safety of the vaccine has been evaluated in several studies in more than 600,000 children (ages 1 to 15 years). Fever occurred in less than 1 in 500, and no associated encephalitis cases emerged. In one study of 25,000 children who were closely followed, the vaccinated group showed no difference in symptoms compared to the control group. This vaccine is produced inexpensively in China.

Studies in China have shown protective efficacy of 96% to 98% up to 17 years after a two-dose regimen. While the present national recommendation is for two doses given one year apart, followed by a booster at age six , this may change in the light of the most recent data showing efficacy of a single dose. A study from Nepal has reported a 99.6% efficacy rate with a single dose given within one week of an outbreak. A further study showed 98.5% protection 12 to 15 months after vaccination.

As no JE vaccine including the SA 14-14-2 vaccine is yet prequalified by WHO, this vaccine is not available for purchase through UN agencies like UNICEF for broader international use, although prequalification is expected in 2008. However, India, South Korea, and Nepal already have licensed this vaccine for use. In Sri Lanka, LJEV has been given provisional registration for use in clinical studies in the public sector.

Recently the Programme for Appropriate Technology in Health [PATH] entered into an agreement with the supplier of live attenuated SA 14-14-2 vaccine and this agreement has enabled the low – income countries who are supported by the Global Alliance of Vaccine & Immunization to have a **public price** for the vaccine. Already India and Nepal has received the benefit of this agreement and they are using the vaccine for a very low price making millions of children protected against JE. The Government of Napal has gone a step beyond and has vaccinated even adults to protect them from this deadly disease.

The price per dose of inactivated JE vaccine for the Sri Lankan government in year 2006 was US$4.50. Given the 3-dose primary series and a booster dose required , the annual cost of JE vaccine in Sri Lanka is now well over three-quarters of the Sri Lankan government's entire budget for all vaccines. Thus, the cost of inactivated JE vaccine is becoming prohibitive and jeopardizing the Sri Lankan government's ability to sustain a public policy of immunization against JE. If LJEV is given full licensure in Sri Lanka, at a price of below US$0.75 LJEV would be a sustainable part of the Sri Lankan immunization programme and also would save the large sum of money for the Sri Lankan public health system annually.

Once the Immunogenecity and safety of the LJEV is confirmed through the results of the ongoing clinical trial done in Colombo , Ministry of Health would be in a very strong position to work out a public price for LJEV vaccine like in India and Nepal, Sri Lanka would thus be able to introduce it to the National EPI programme and protect its adult population too from this deadly disease and also it would be an important landmark in the history of immunization in Sri Lanka

Sources

Proceedings of the Sri Lanka National Immunization Summit—2007 , Epidemiology Unit , Ministry of Health Sri Lanka.

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Table 1: Vaccine-preventable Diseases & AFP

8th – 14th March 2008 (11th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2008	Number of cases during same week in 2007	Total number of cases to date in 2008	Total number of cases to date in 2007	Difference between the number of cases to date between 2008 & 2007
	W	C	S	N	E	NW	NC	U	Sab					
Acute Flaccid Paralysis	00	00	00	00	00	00	00	00	00	00	03	17	18	+5.6%
Diphtheria	00	00	00	00	00	00	00	00	00	00	00	00	00	00.0%
Measles	00	00	00	00	00	00	00	00	00	00	01	26	12	+116.7%
Tetanus	00	00	00	00	00	00	00	00	00	00	00	08	09	-11.1%
Whooping Cough	00	00	00	00	00	01 KR=1	00	00	00	01	02	08	12	-33.3%
Tuberculosis	91	02	11	01	05	11	05	00	00	126	145	1935	2044	-5.3`%

Table 2: Newly Introduced Notifiable Diseases

8th – 14th March 2008 (11th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2008	Number of cases during same week in 2007	Total number of cases to date in 2008	Total number of cases to date in 2007	Difference between the number of cases to date between 2008 & 2007
	W	C	S	N	E	NW	NC	U	Sab					
Chicken-pox	25	08	12	15	03	02	01	10	25	101	64	1206	659	+83.0%
Meningitis	01 GM=1	00	04 GL=3 HB=1	01 JF=1	01 TR=1	05 KR=4 PU=1	03 PO=3	0I BD=1	07 RP=3 KG=4	23	00	392	46	+752.2%
Mumps	04	17	03	00	04	02	00	01	07	38	24	477	160	+198.1%

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.
DPDHS 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.

Table 3: Laboratory Surveillance of Dengue Fever

8th – 14h March 2008 (11th Week)

Samples	Number tested		Number positive *		Serotypes									
					D_1		D_2		D_3		D_4		Negative	
	GT	AH	GT	AH	GT	AH	GT	AH	GT	AH	GT	AH	GT	AH
Number for current week	03	02	00	00	00	00	00	00	00	00	00	00	00	00
Total number to date in 2008	39	21	04	06	00	00	02	02	00	00	00	00	02	00

Sources: Genetech Molecular Diagnostics & School of Gene Technology, Colombo [GT] and Genetic Laboratory Asiri Surgical Hospital [AH]
* Not all positives are subjected to serotyping.
NA= Not Available.

Data Sources:
Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Whooping Cough, Human Rabies, Dengue Haemorrhagic Fever, Japanese Encephalitis, Chickenpox, Meningitis, Mumps.
Special Surveillance: Acute Flaccid Paralysis.
National Control Program for Tuberculosis and Chest Diseases: Tuberculosis.

Table 4: Selected notifiable diseases reported by Medical Officers of Health

8th – 14th March 2008 (11th Week)

DPDHS Division	Dengue Fever / DHF*		Dysentery		Encephal-itis		Enteric Fever		Food Poisoning		Leptos-pirosis		Typhus Fever		Viral Hepatitis		Human-Rabies		Returns Re-ceived Timely**
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	%
Colombo	26	400	01	36	00	04	03	41	03	56	05	39	00	00	02	29	00	01	**69**
Gampaha	12	266	05	37	00	03	00	17	00	16	09	55	00	01	00	37	00	00	**57**
Kalutara	11	134	08	95	00	06	06	32	00	11	21	72	00	02	01	14	00	00	**100**
Kandy	08	61	08	60	01	02	01	12	00	08	03	46	07	24	05	49	00	00	**67**
Matale	01	26	06	61	00	00	01	12	00	00	05	129	00	01	00	11	00	00	**58**
Nuwara Eliya	00	05	06	47	00	00	02	66	00	62	00	10	03	24	03	45	00	01	**38**
Galle	02	31	02	32	01	07	01	10	04	42	06	66	00	06	01	04	00	02	**71**
Hambantota	00	38	01	26	00	02	01	05	00	06	03	27	01	25	00	03	00	00	**91**
Matara	07	68	02	53	00	02	04	19	00	02	19	62	08	55	00	02	00	01	**76**
Jaffna	00	29	04	34	00	00	10	106	00	02	00	00	08	91	01	17	00	00	**75**
Kilinochchi	00	00	00	01	00	00	00	00	00	00	00	01	00	00	00	01	00	00	**00**
Mannar	00	10	00	01	00	06	00	68	00	00	00	00	00	00	00	08	00	00	**00**
Vavuniya	00	10	01	10	00	01	00	01	00	04	00	00	00	00	00	02	00	00	**75**
Mullaitivu	00	00	00	01	00	00	00	05	00	00	00	00	00	00	00	04	00	00	**00**
Batticaloa	03	46	00	19	00	00	00	04	00	03	00	00	01	01	00	40	00	02	**27**
Ampara	00	06	00	62	00	00	00	01	00	00	00	05	00	00	00	01	00	00	**14**
Trincomalee	00	94	01	21	00	00	00	04	00	01	01	06	00	09	00	08	00	00	**40**
Kurunegala	03	125	01	98	00	05	00	16	01	02	01	12	00	11	01	13	00	01	**50**
Puttalam	13	147	02	28	00	01	01	37	00	03	00	02	02	11	00	14	00	01	**56**
Anuradhapur	04	75	01	20	00	03	00	04	00	04	00	23	00	07	01	05	00	00	**53**
Polonnaruwa	02	26	00	31	00	01	04	13	00	04	01	07	00	00	00	10	00	00	**71**
Badulla	00	17	05	106	01	03	06	32	00	01	00	06	02	31	03	46	00	01	**60**
Monaragala	02	20	01	51	00	01	01	11	01	08	00	15	07	37	01	07	00	00	**82**
Ratnapura	02	82	01	58	00	13	02	34	00	42	02	27	00	45	01	26	00	00	**69**
Kegalle	08	80	07	132	00	13	02	10	00	00	03	25	02	22	10	114	00	00	**82**
Kalmunai	01	05	07	49	00	00	00	00	00	03	00	00	00	01	00	10	00	00	**54**
SRI LANKA	**105**	**1801**	**70**	**1169**	**03**	**73**	**45**	**560**	**09**	**280**	**79**	**635**	**41**	**404**	**30**	**520**	**00**	**10**	**60**

Source: Weekly Returns of Communicable Diseases (WRCD).
***Dengue Fever / DHF** refers to Dengue Fever / Dengue Haemorrhagic Fever.
****Timely** refers to returns received on or before 22 March , 2008 Total number of reporting units =290. Number of reporting units data provided for the current week: 238

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