WEEKLY EPIDEMIOLOGICAL REPORT

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Ministry of Health

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Vaccine Adjuvants

A vaccine adjuvant may be defined as any substance that, when incorporated into a vaccine formulation, acts generally to accelerate, prolong or enhance the quality of specific immune responses to vaccine antigens. The word adjuvant is derived from the Latin verb adjuvare, which means to help or aid. Adjuvant mechanisms of action include the following:

* Increasing the biological or immunologic half -life of vaccine antigens
* Improving antigen delivery to antigen-presenting cells (APCs), as well as antigen processing and presentation by the APCs
* Inducing the production of immunomodulatory cytokines. Through modulation of cytokine responses, adjuvant formulations can be designed that favour the development of T-helper type 1 (Th1) or type 2 (Th2) immune responses to vaccine antigens.

Novel adjuvants are presently undergoing preclinical and clinical testing with human candidate vaccines, including experimental subunit vaccines against tuberculosis.

Vaccine adjuvants have been in the process of being developed and tested for most of this century. In the mid-1920s, it was observed that horses which developed abscesses at the injection site produced higher antitoxin titers than horses without abscesses. In 1926, the adjuvant activity of aluminum compounds with the use of an alum-precipitated diphtheria toxoid vaccine was demonstrated.

Presently, aluminum salt based adjuvants continue to be the most commonly used immunologic adjuvant. However, hundreds of natural and synthetic compounds that have adjuvant activity have been identified. A number of these novel adjuvants, which may be used to augment or replace alum in human vaccines, have been under development and in preclinical evaluation for several decades. In animal models, many novel adjuvants have been demonstrated to be more effective than alum in enhancing both antibody and cell-mediated immune responses to vaccine antigens. Extensive preclinical evaluation of novel immunologic adjuvants have been conducted and clinical trials comparing the activities of various adjuvants have been initiated.

Advantages of Adjuvant use

Potential advantages of the use of immunologic adjuvants in vaccine formulations include their ability

* To direct and optimize immune responses that are appropriate for the vaccine
* To enable mucosal delivery of vaccines
* To promote cell-mediated immune responses
* To enhance the immunogenicity of weaker immunogens, such as highly purified or recombinant antigens
* To reduce the amount of antigen or the frequency of immunization required to provide protective immunity
* To improve the efficacy of vaccines in individuals with reduced or weakened immune responses, such as newborns, the aged and immunocompromised vaccine recipients.

Mechanisms of Action

Adjuvants have diverse mechanisms of action and must be chosen for use with a particular vaccine on the basis of the route of administration to be employed and the type of immune responses desired. The first mechanism of adjuvant action identified was the so-called depot effect, in which gel-type adjuvants, such as aluminium hydroxide or emulsion-based adjuvants, such as Freund's incomplete adjuvant, associate with antigen and facilitate transport of antigen to the draining lymph node, where immune responses are generated. Immunogenicity of small antigens such as synthetic peptides that otherwise would be rapidly cleared from the injection site and from draining lymph nodes can be improved by the use of adjuvants that form particles or otherwise associate with and hold antigen.

Adjuvants can also act through enhancement of antigen presentation. Immunologic adjuvants act directly or indirectly on APCs, such as macrophages and

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dendritic cells. The emulsion-based adjuvant MF59 has recently been shown to be internalized by dendritic cells. Certain novel adjuvants, such as purified saponins, immune-stimulatory complexes and liposomes have been shown to greatly improve the induction of major histocompatibility complex (MHC) class I restricted CD8+ cytotoxic T lymphocyte (CTL) responses over that induced by the same antigen given alone or in combination with standard alum adjuvants.

These adjuvants may induce CTL responses by delivering antigen directly to the cytosol for presentation with MHC class I molecules. Cytosolic antigen delivery by membrane-active adjuvants could mimic antigen presentation that occurs during viral infection or immunization with live-attenuated vaccines. Antigen presented to the cytosol could bypass endosomal antigen delivery and subsequent processing with MHC class II molecules, which occurs when antigen is delivered alone or in alum and induces primarily antibody responses via presentation to CD4+ T helper lymphocytes. Adjuvants may also promote cytosolic antigen delivery and MHC class I presentation by enabling antigen to cross endosomal membranes into the cytosol after ingestion of antigen-adjuvant complexes by APCs.

Antigen can be targeted to macrophages or dendritic cells by particulate adjuvants such as liposomes. APCs can also be stimulated by adjuvants to secrete immunomodulatory cytokines. Various cytokines induced by adjuvants act on lymphocytes to promote predominately Th1 or Th2 immune responses. Adjuvants that enhance Th1 immune responses through the induction of IFN-γ and delayed-type hypersensitivity also elicit the production of IgG subclasses that fix complement and bind with high affinity to Fc-γ-I receptors (e.g., IgG2a in mice and IgG1 in humans). These immunoglobulin subclasses are the most active in complement-mediated lysis and in antibody-dependent cell-mediated—cytotoxicity effector mechanisms.

Several cytokines are under evaluation as vaccine adjuvants, including IL-2, IFN-γ granulocyte-macrophage colony stimulating factor, and IL-12. IL-12 is a recently characterized cytokine that may play a pivotal role in the immunomodulatory activities of various immunologic adjuvants. Jankovic et al. showed that the addition of IL-12 to an alum-adsorbed HIV-1 gp120 vaccine elicited Th1 cytokines and IgG2 and IgG3 antibody responses in mice; the same vaccine without IL-12 induced Th2 cytokines and IgG1 antibody responses. Bacterial toxins with adjuvant activity, such as cholera toxin and pertussis toxin, which preferentially drive Th2-like responses, have been shown to enhance IgA and IgE antibody production. Adjuvants that drive Th2-like immune responses could enhance protection against mucosal virus transmission by augmenting IgA production.

Adjuvant Safety

The benefits of incorporating adjuvants into vaccine formulations to enhance immunogenicity must be weighed against the risk that these agents will induce adverse reactions. Local adverse reactions include local inflammation at the injection site and, rarely, the induction of granuloma or sterile abscess formation. Systemic reactions to adjuvants observed in laboratory animals include malaise, fever, adjuvant arthritis and anterior uveitis. Such reactions often are caused by the interaction of the adjuvant and the antigen itself, or may be due to the type of response to a particular antigen the adjuvant produces, or the cytokine profile the adjuvant produces in an antigen. Therefore, even though separate and extensive preclinical toxicological and safety studies have been performed on both the adjuvant and the vaccine antigens, a final safety evaluation of the human candidate vaccine formulation proposed for phase I clinical testing should be conducted.

Future Directions

Adjuvant research is a field that is advancing rapidly, with the discovery of new adjuvants and better understanding of immune mechanisms. Adjuvants can also be employed in vaccine design research, which could assist in identifying the requirements of protective immunity, since different adjuvants vary immune responses to the same experimental antigen.

Source-Improving Vaccine Performance with Adjuvants,

available from http://cid.oxfordjournals.org/content/30/Supplement_3/S266.full#sec-3

Compiled by Dr. Madhava Gunasekera of the Epidemiology Unit

Water Quality Surveillance
Number of microbiological water samples - January / 2013

District	MOH areas	No: Expected *	No: Received
Colombo	12	72	61
Gampaha	15	90	15
Kalutara	12	72	43
NHIS	2	12	22
Kandy	23	138	0
Matale	12	72	0
Nuwara Eliya	13	78	0
Galle	19	114	NR
Matara	17	102	0
Hambantota	12	72	30
Jaffna	11	66	70
Kilinochchi	4	24	8
Manner	5	30	19
Vavuniya	4	24	37
Mullatvu	4	24	0
Batticaloa	14	84	NR
Ampara	7	42	NR
Trincomalee	11	66	NR
Kurunegala	23	138	49
Puttalam	9	84	NR
Anuradhapura	19	114	23
Polonnaruwa	7	42	13
Badulla	15	90	105
Moneragala	11	66	44
Rathnapura	18	108	NR
Kegalle	11	66	18
Kalmunai	13	78	NR

* No of samples expected (6 / MOH area / Month)
NR = Return not received

Table 1: Vaccine-preventable Diseases & AFP

09th – 15th February 2013 (07th 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					
Acute Flaccid Paralysis	00	00	00	00	01	00	00	00	00	01	02	10	11	- 09.0 %
Diphtheria	00	00	00	00	00	00	00	00	00	-	-	-	-	-
Measles	05	00	00	01	00	00	00	00	00	06	00	33	06	+ 450.0 %
Tetanus	00	00	00	00	00	00	00	00	00	00	01	02	02	%
Whooping Cough	00	00	00	00	00	00	00	00	00	01	02	07	12	- 41.7 %
Tuberculosis	148	24	20	16	08	52	29	16	35	348	130	1253	1295	- 03.2 %

Table 2: Newly Introduced Notifiable Disease

09th – 15th February 2013 (07th 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					
Chickenpox	16	05	12	00	02	15	04	01	03	58	131	484	674	- 28.2 %
Meningitis	04 CB=3 KL=1	00	07 MT=5 HB=1 GL=1	01 KN=1	01 AP=1	02 KG=1 PU=1	01 AP=1	00	02 RP=2	18	11	139	114	+ 21.9 %
Mumps	01	00	00	01	02	04	01	00	03	12	70	179	559	- 69.8 %
Leishmaniasis	00	00	00	01 VU=1	01 AM=1	00	04	00	00	06	15	142	129	+ 10.0 %

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.

Data Sources:

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

Special Surveillance: Acute Flaccid Paralysis.

Leishmaniasis is notifiable only after the General Circular No: 02/102/2008 issued on 23 September 2008. .

Influenza Surveillance in Sentinel Hospitals - ILI & SARI									
Month	Human						Animal		
	No Received	Infl A untyped	Infl B	A(H1N1)pdm09	A(H3N2)	RSV	Pooled samples	Serum Samples	Positives
January	312	07	29	33	44	0	174	147	0

Source: Medical Research Institute & Veterinary Research Institute

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.

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

09th – 15th February 2013 (07th Week)

DPDHS Division	Dengue Fever / DHF*		Dysentery		Encephalitis		Enteric Fever		Food Poisoning		Leptospirosis		Typhus Fever		Viral Hepatitis		Human Rabies		Returns Received
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	%
Colombo	172	1251	4	27	0	5	1	21	0	9	5	26	0	1	0	9	0	0	**46**
Gampaha	46	593	1	17	0	4	0	8	0	1	3	18	0	5	5	38	0	0	**27**
Kalutara	22	238	4	29	1	6	1	13	0	4	2	45	0	1	0	3	0	0	**31**
Kandy	29	242	0	9	0	0	0	1	0	0	0	3	0	1	0	3	0	0	**22**
Matale	0	58	3	18	0	0	0	0	0	0	0	4	0	1	1	10	0	0	**50**
NuwaraEliya	6	38	1	11	1	1	0	1	0	1	0	1	3	16	0	0	0	0	**46**
Galle	6	83	0	8	0	4	0	0	0	2	0	14	1	8	0	2	0	0	**32**
Hambantota	8	51	1	9	0	0	0	3	1	2	9	41	0	15	1	26	0	0	**67**
Matara	27	103	2	5	2	5	0	1	0	3	7	20	4	10	1	55	0	1	**94**
Jaffna	12	133	3	30	0	1	4	72	0	0	0	2	5	91	0	3	0	0	**42**
Kilinochchi	1	5	1	4	0	0	1	3	0	1	0	1	0	0	0	0	0	0	**0**
Mannar	3	32	3	12	0	1	7	20	0	11	0	4	0	3	0	0	0	0	**60**
Vavuniya	2	17	2	13	0	5	0	2	1	4	1	8	1	1	0	0	0	0	**25**
Mullaitivu	0	13	1	2	0	0	0	1	0	0	0	2	0	2	0	0	0	0	**60**
Batticaloa	6	92	1	19	0	1	0	0	0	0	0	5	0	0	0	3	0	0	**86**
Ampara	1	21	1	23	0	0	0	1	0	0	1	4	0	0	0	1	0	0	**29**
Trincomalee	8	51	0	7	0	0	0	0	0	0	1	12	0	1	1	1	0	0	**58**
Kurunegala	39	929	3	33	0	7	0	10	0	1	0	13	0	7	1	11	0	0	**46**
Puttalam	33	249	1	10	0	1	0	2	0	1	0	3	0	0	0	0	0	0	**33**
Anuradhapu	5	103	1	11	0	6	0	0	0	0	3	26	0	4	0	2	0	0	**32**
Polonnaruw	1	46	1	19	0	2	0	3	0	0	1	41	0	0	0	3	0	0	**29**
Badulla	12	72	1	19	0	2	0	3	0	0	1	4	0	4	1	7	0	0	**41**
Monaragala	1	31	1	13	0	1	0	3	0	0	4	23	1	6	2	12	0	0	**64**
Ratnapura	20	200	5	65	3	52	0	7	0	7	1	34	1	5	7	62	0	1	**50**
Kegalle	14	189	1	7	0	9	0	2	0	2	2	10	0	9	6	38	0	0	**36**
Kalmune	5	149	0	14	0	1	0	0	0	4	0	3	0	0	0	2	0	0	**23**
SRI LANKA	**479**	**4990**	**42**	**434**	**07**	**110**	**14**	**177**	**02**	**53**	**41**	**365**	**16**	**191**	**26**	**291**	**00**	**02**	**44**

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 01st February, 2013 Total number of reporting units 336. Number of reporting units data provided for the current week: 169
A = Cases reported during the current week. **B** = Cumulative cases for the year.

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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.**

ON STATE SERVICE

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