WEEKLY EPIDEMIOLOGICAL REPORT

A publication of the Epidemiology Unit
Ministry of Health

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

Vol. 40 No.42 — 12th – 18th October 2013

WER SRI LANKA- 2013

Causality Assessment of AEFI (Part II)

This is the second in a series of two articles on Causality Assessment of Adverse Events Following Immunization (AEFI)

The individual level

At the individual level it is usually not possible to establish a definite causal relationship between a particular AEFI and a particular vaccine on the basis of a single AEFI case report. However, it is important to try in order to identify a possible new vaccine product related AEFI, as well as to determine if the event is preventable or remedial such as a product-related quality defect or immunization error. Identifying a coincidental AEFI that is falsely attributed to a vaccine product is vital as otherwise the coincidence may result in loss of public confidence in the vaccine, with the consequent return of vaccine-preventable disease.

The aim of causality assessment at the individual level is to address the question "Did the vaccine given to a particular individual cause the particular event reported? As noted, it is seldom possible to achieve a straightforward answer to this question, so in most cases the assessment involves systematic consideration of all possible causes of an AEFI in order to arrive at a conclusion that the evidence is consistent with the vaccine being a cause, or is inconsistent with this conclusion, or is indeterminate.

* The scientific basis for the criteria which are assessed in the process include:
* Temporal relationship: The vaccine exposure must precede the occurrence of the event.
* Definitive proof that the vaccine caused the event: Clinical or laboratory proof that the vaccine caused the event is most often found for live attenuated vaccines. (For instance, in a case of aseptic meningitis after immunization with Urabe mumps vaccine virus, isolation of the Urabe virus from the cerebrospinal fluid is definitive proof that it caused the meningitis. Another example is isolation of the BCG agent from a focus of osteomyelitis.)
* Population-based evidence for causality – i.e. what is known about "Can it?"

A definitive "yes" at the population level is consistent with causality at the individual level.
A strong "no" at the population level is inconsistent with causality at the individual level.

If there is no clear answer to the question at the population level, this will often lead to an indeterminate conclusion at the individual level. If there are significant numbers of individual cases, however, this clearly points to the need to try to answer the question at the population level.

* Biological plausibility: In situations where the "Can it?" question has no clear "yes "or "no" answer, biological plausibility may provide support for or against vaccine causality. In other words, the association should be compatible with existing theory and knowledge related to how the vaccine works.
* Consideration of alternative explanations: In doing causality assessment on an individual case report, it must be remembered that in essence one is conducting a differential diagnosis. Thus it is important to consider "coincidental AEFI" – i.e. an AEFI due to something other than the vaccine product, immunization error or immunization anxiety. All reasonable alternative etiological explanations should be considered, including:
* preexisting illness
* newly acquired illness
* spontaneous occurrence of an event without known risk factors
* emergence of a genetically programmed disease
* other exposures to drugs or toxins prior to the event
* surgical or other trauma that leads to a complication
* a manifestation of, or complication of, a coincidental infection that was present before or at the time of immunization, or was incubating, but was not apparent at the time of immunization.
* Prior evidence that the vaccine in question could cause a similar event. The concept of "rechallenge", which is more commonly used in the assessment of causality in medicines, has been helpful for certain vaccine event considera-

Contents	Page

tions (e.g. GuillainBarré syndrome (GBS) after tetanus toxoid vaccination, where GBS occurred on three separate occasions in the same individual within weeks of administration of tetanus toxoid)

Investigation of signals

The assessment of whether a particular vaccine is likely to cause a particular AEFI takes into account all evidence from individual cases of AEFI, as well as surveillance data and, where applicable, cluster investigations and nonclinical data.

Case selection for causality assessment

The selection of cases for causality assessment should focus on

* serious AEFI1 that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect
* the occurrence of events above the expected rate or of unusual severity
* signals generated as a result of individual or clustered cases as these could signify a potential for large public health impact.
* WHO recommends that other AEFI should also be assessed if the reviewing team or review committee decides that causality needs to be determined as a special case or in order to conduct special studies. Such AEFI could include:
* AEFI that may have been caused by immunization error (e.g. bacterial abscess, severe local reaction, high fever or sepsis, BCG lymphadenitis, toxic shock syndrome)
* significant events of unexplained cause occurring up to 30 days after a vaccination (and that are not listed on the product label)
* events causing significant parental or community concern (e.g. hypotonic hyporesponsive episode (HHE), febrile seizures).

Prerequisites for causality assessment

* AEFI are usually reported through passive or stimulated passive surveillance, and less frequently from active surveillance systems. Timely reporting of AEFI followed by appropriate and detailed investigation is the key to successful causality assessment and signal detection. An AEFI report should fulfill three prerequisites before causality assessment, namely:
* The AEFI case investigation should have been completed. Premature assessments with inadequate information could mislead the classification of the event.
* All details of the case should be available at the time of assessment. Details should include documents pertaining to the investigation as well as laboratory and autopsy findings as appropriate.
* There must be a "valid diagnosis" (as explained below) for the unfavourable or unintended sign, abnormal laboratory finding, symptom or disease in question.

Who should do causality assessment?

To ensure that the prerequisite criteria described above are met and to ensure broader acceptance of the findings, causality assessment of AEFI should ideally be performed by a reviewing team or committee of reviewers from relevant specialties. However, in many countries and situations this broad level of expertise may not be available and existing human resources need to be used for the causality assessment of AEFI.

Steps for causality assessment of an individual adverse event

The revised process envisages the causality assessment of an individual AEFI case in relation to a particular vaccine. If multiple vaccines are given simultaneously, the reviewers will have to assess causality separately for each suspected vaccine.

Causality assessment has four steps, as follows:

Step 1: Eligibility. The first step aims to determine if the AEFI case satisfies the minimum criteria for causality assessment as outlined below.

* Step 2: Checklist. The second step involves systematically reviewing the relevant and available information to address possible causal aspects of the AEFI.
* Step 3: Algorithm. The third step obtains a trend as to the causality with the information gathered in the checklist.
* Step 4: Classification. The fourth step categorizes the AEFI's association to the vaccine or vaccination on the basis of the trend determined in the algorithm.

Step 1: Eligibility

Before proceeding with causality assessment, it is necessary first to confirm that the vaccine was administered before the event occurred. This can be ascertained by eliciting from the relevant informants a very detailed and careful history and physical findings. It is also essential to have a valid diagnosis for the reported AEFI, which could be an unfavourable or unintended sign, an abnormal laboratory finding, a symptom or a disease.

Step 2: Checklist

The checklist is designed to assemble information on the patient-immunization-AEFI relationship in the following key areas:

* evidence for other causes
* association of the event and the vaccine/vaccination with the vaccine product(s), immunization error or immunization anxiety (if there is an association, it is important to find out if the event occurred within an appropriate time window)
* evidence against a causal association
* other qualifying factors for classification such as the background rate of the event, present and past health condition, potential risk factors, medication,biological plausibility etc.

Step 3: Algorithm

After the checklist is completed, the AEFI case is ready to be applied to the algorithm. The algorithm aims to be a roadmap for the decision-making of the reviewers but it does not, and should not, take away the expert and deductive logical process inherent in linking a diagnosis to its potential cause. The stepwise approach of the algorithm helps to determine if the AEFI could be consistent or inconsistent with an association to immunization, an indeterminate outcome or unclassifiable

Step 4: Classification

The final classification has been adapted from Definition and application of terms for vaccine pharmacovigilance. Report of the CIOMS/WHO Working Group on Vaccine Pharmacovigilance. The cause-specific definitions provide clarity on "A. Consistent causal association to immunization" and "C. Inconsistent causal association to immunization" (coincidental). The association is considered "B. indeterminate" when adequate information on the AEFI is available but it is not possible to assign it to either of the above categories.

More information on causality assessment is available from The World Health Organization (from the web link mentioned below)

Source-Causality assessment of AEFI following Immunization- available from *http://www.who.int/vaccine_safety/publications/aevi_manual.pdf*

Compiled by Dr. Madhava Gunasekera of the Epidemiology Unit

Table 4: Selected notifiable diseases reported by Medical Officers of Health 05th – 11th October (41stWeek)

RDHS	Dengue Fever		Dysentery		Encephaliti		E Fever		F Poisoning		Leptospirosi		T Fever		V Hepatitis		H Rabies		Chickenpox		Meningitis		Leishmania-		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	57	7771	3	171	0	17	2	126	1	53	1	179	0	7	3	71	0	1	5	364	3	59	0	0	**54**	**46**
Gampaha	53	2978	1	171	1	16	0	45	2	31	12	342	2	18	2	167	0	0	1	142	1	82	0	5	**80**	**20**
Kalutara	14	1456	1	153	0	19	1	70	0	23	4	337	0	5	0	20	0	0	1	226	1	64	0	0	**38**	**62**
Kandy	7	1513	1	133	0	11	0	24	2	10	3	68	1	94	9	98	0	0	7	119	0	14	0	4	**74**	**26**
Matale	0	400	1	84	0	4	0	24	0	7	0	57	0	4	0	44	0	0	0	43	0	33	0	11	**46**	**54**
NuwaraEliya	2	214	3	140	0	2	2	13	0	217	0	24	0	57	0	20	0	0	5	106	0	12	0	0	**69**	**31**
Galle	4	748	1	100	0	19	1	6	0	81	0	193	0	51	0	13	0	2	4	279	0	45	0	0	**68**	**32**
Hambantota	2	283	0	48	0	3	0	15	0	32	0	159	1	62	0	83	0	0	1	92	0	44	0	274	**50**	**50**
Matara	4	406	2	71	0	12	0	28	0	27	4	136	1	78	2	136	0	2	4	235	1	70	0	78	**94**	**6**
Jaffna	9	593	28	324	0	10	2	299	0	96	0	8	1	329	0	17	0	1	1	132	1	54	0	0	**83**	**17**
Kilinochchi	0	57	0	33	0	0	0	14	0	5	0	9	0	16	0	0	0	2	0	2	0	7	0	11	**0**	**100**
Mannar	0	65	0	68	0	3	0	59	0	36	0	14	0	19	0	2	0	0	0	11	0	5	0	4	**0**	**100**
Vavuniya	1	64	7	55	0	13	0	12	1	20	0	50	0	2	0	3	0	2	0	22	1	33	1	10	**50**	**50**
Mullaitivu	3	110	0	19	0	2	0	8	0	43	0	37	0	6	0	1	0	2	0	8	0	6	0	14	**40**	**60**
Batticaloa	5	503	2	267	0	5	0	10	0	72	0	33	0	2	0	13	0	3	1	40	0	7	0	0	**29**	**71**
Ampara	2	170	9	149	0	1	0	5	0	10	0	33	0	1	0	8	0	0	3	81	0	17	0	3	**86**	**14**
Trincomalee	0	183	0	59	0	3	0	5	0	3	0	59	1	15	0	3	0	1	0	37	0	4	0	28	**42**	**58**
Kurunegala	22	2499	3	156	1	36	0	38	3	26	8	282	1	41	2	52	0	1	2	317	0	94	3	43	**70**	**30**
Puttalam	5	800	2	65	0	7	0	16	0	36	1	42	0	12	0	6	0	1	0	76	0	31	0	8	**38**	**62**
Anuradhapur	5	462	5	96	0	16	0	3	0	40	1	302	0	23	0	24	0	2	2	159	1	90	8	354	**58**	**42**
Polonnaruwa	10	384	1	70	0	1	0	14	0	62	1	158	0	3	1	29	0	2	2	121	0	17	1	144	**57**	**43**
Badulla	5	443	4	172	0	5	0	17	0	10	0	53	3	77	0	43	0	0	2	110	3	60	0	7	**65**	**35**
Monaragala	2	213	3	105	0	4	1	23	0	25	0	196	3	56	0	156	0	1	1	48	0	23	0	10	**45**	**55**
Ratnapura	5	1567	3	321	0	83	0	37	0	16	2	305	0	62	6	398	0	1	3	148	0	74	0	12	**39**	**61**
Kegalle	13	962	0	110	0	15	2	28	0	11	8	194	2	71	12	201	0	0	2	281	0	99	1	2	**55**	**45**
Kalmune	1	491	0	136	0	2	0	3	0	117	0	8	0	2	0	5	0	0	0	82	0	9	0	1	**23**	**77**
SRI LANKA	**231**	**25335**	**80**	**3276**	**02**	**309**	**11**	**942**	**09**	**1109**	**45**	**3278**	**16**	**1113**	**37**	**1613**	**00**	**24**	**47**	**3281**	**12**	**1053**	**14**	**1023**	**57**	**43**

Source: Weekly Returns of Communicable Diseases (WRCD).

*T=Timeliness refers to returns received on or before 11th October , 2013 Total number of reporting units 339. Number of reporting units data provided for the current week:266 C** 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 05th – 11th October 2013 (41st 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*	00	00	00	00	00	00	00	02	02	04	04	76	64	+ 18.7 %
Diphtheria	00	00	00	00	00	00	00	00	00	-	-	-	-	-
Mumps	00	04	00	00	08	02	01	00	02	17	41	1256	3823	- 67.1 %
Measles	20	01	10	00	01	05	01	01	15	54	01	3147	50	+ 6194.0 %
Rubella	00	00	00	00	00	00	00	00	00	00	-	25	-	-
CRS**	00	00	00	00	00	00	00	00	00	00	-	06	-	-
Tetanus	00	00	00	00	00	00	00	00	00	00	00	19	11	+ 72.7 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	-	00	-	-
Japanese Encephalitis	01	00	00	00	00	00	00	00	00	01	-	67	-	-
Whooping Cough	00	00	00	00	00	01	00	00	00	01	00	69	86	- 19.7 %
Tuberculosis	29	15	40	16	16	14	28	04	49	211	136	6597	6823	- 03.3 %

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.

PRINTING OF THIS PUBLICATION IS FUNDED BY THE WORLD HEALTH ORGANIZATION (WHO).

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