Adverse events following immunisation (AEFI) with 2010/2011 seasonal influenza vaccines

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1. Introduction

Since October 1st 2010, Lareb received 146 reports of one or more adverse events attributed by the reporter to vaccination with seasonal influenza vaccine. One report concerned the death of a vaccinee. An additional 10 reports concerned serious events according to CIOMS criteria. These 11 reports are discussed in more detail below. An additional 7 reports of special interest such as potential serious hypersensitivity reactions, or reactions in which the reported event may consist of an immune disorder are presented. One other report concerning a serious event associated with 2009/2010 seasonal influenza vaccination (reported to Lareb in December 2010) is also presented. All reports of serious events and events of special interest are shown in more detail in Annex A.

2. Results

In total 240 events, shown in Table 1, were reported related to 2010/2011 seasonal influenza vaccination in 146 subjects. 103 (71%) of the report concerned female patients, 43 (29%) concerned males. Ages ranged from 1 year to 88 years; age was unknown in two cases. 56 Vaccinees were aged sixty years or more, 84 vaccinees were aged less than 60 years and were vaccinated due to medical risk factors. In 77 reports one event was coded, in the remaining 69 cases more events were reported. Events are listed as coded. This implies that different terms may have been used to describe more or less the same symptoms. In this report only reported events are presented, without assessment of causality. This is only shown for cases presented in more detail. The reports originated from consumers in 92 cases, general practitioners in 35 cases, medical specialists in 13 cases, 4 from not specified physicians and one from a pharmacist. In two cases no source was specified.
Serious events were not associated with specific vaccine brands or batches.

Table 1 Reported events after vaccination with influenza vaccines 2010/2011, grouped by system organ class (MedDRA)

System Organ Class	N	Preferred term
Blood and lymphatic system disorders, n=6	5	Lymphadenopathy
	1	Thrombocytopenia
Cardiac disorders, n=4	1	Chest pain
	1	Palpitations
	1	Peripheral oedema
	1	Myocardial infarction
Eye disorders, n=3	1	Conjunctivitis
	1	Eye pain
	1	Eye irritation
Gastrointestinal disorders, n =18	4	Diarrhoea
	1	Flatulence
	1	Lip swelling
	3	Nausea
	2	Abdominal discomfort
	1	Abdominal distension
	1	Abnormal faeces
	2	Vomiting
	1	Swollen tongue
	1	Abdominal pain upper
	1	Glossitis

System Organ Class	N	Preferred term
General disorders and administration site, n=104	1	Death
	3	Application site reaction
	1	Asthenia
	2	Fatigue
	1	Feeling abnormal
	2	Feeling hot
	2	Inflammation
	15	Influenza like illness
	1	Injection site atrophy
	2	Injection site induration
	1	Injection site infection
	37	Injection site inflammation
	4	Injection site pain
	1	Injection site pruritus
	5	Injection site reaction
	8	Malaise
	1	Mucosal inflammation
	1	Chills
	2	Pain
	14	Pyrexia
Immune system disorders, n=2	1	Hypersensitivity
	1	Sarcoidosis
Infections and infestations, n=7	1	Nasopharyngitis
	1	Herpes zoster
	2	Pharyngitis
	1	Respiratory tract Infection
	1	Cystitis
	1	Erysipelas
Injury, poisoning and procedural complications, n=1	1	Blister
Investigations, n=2	1	Blood pressure increased
	1	Body temperature increased
Musculoskeletal and connective tissue disorders, n=20	4	Arthralgia
	1	Monoarthritis
	1	Muscle twitching
	1	Muscular weakness
	6	Myalgia
	2	Neck pain
	2	Pain in extremity
	2	Rheumatoid arthritis
	1	Sensation of heaviness
Nervous system disorders, n=34	1	Disturbance in attention
	6	Dizziness
	1	Dysgeusia
	1	Epilepsy
	16	Headache
	2	Hypoaesthesia
	1	Migraine
	1	Multiple sclerosis
	2	Paraesthesia
	3	Syncope
Pregnancy, puerperium and perinatal conditions, n=1	1	Suppressed lactation
Psychiatric disorders n=1	1	Apathy
Respiratory, thoracic and mediastinal disorders, n=12	2	Asthma
	3	Cough
	3	Dyspnoea
	1	Dyspnoea exertional
	1	Neonatal hypoxia
	2	Oropharyngeal pain

System Organ Class	N	Preferred term
Skin and subcutaneous tissue disorders, n=20	1	Angioedema
	1	Blister
	2	Dermatitis Bullous
	1	Eczema
	1	Erythema
	1	Face Oedema
	1	Night sweats
	5	Pruritus
	2	Rash
	1	Rash papular
	1	Rash pruritic
	1	Skin exfoliation
	1	Swelling face
	1	Urticaria
Vascular disorders, n=5	1	Arterial thrombosis
	1	Haematoma
	1	Lymphangitis
	1	Pallor
	1	Transient ischaemic attack
TOTAL no of reported events	240	

3. General overview of non-serious events

Events were classified into serious and non-serious events according to established CIOMS criteria. The reported non-serious events predominately consist of well known adverse reactions. Local reactions (51) represent one fifth of the reported events. Headache, influenza-like illness, myalgia, pyrexia and malaise account for an additional sixty events. Other events were reported less often: apart from dizziness (n=6), no other events exceed five reports.

4. Serious events

Serious events are listed in Table 2 and commented in the text below.

Fatalities. One case (A) concerns an unexpected, unexplained death 12 to 36 hours after vaccination. Patient (healthy, minor medical history) attended a social meeting the evening after vaccination, and was apparently in good health, but did not respond to contact the following day. One day later his house was entered, where the vaccinee was found dead. No autopsy has been performed. Examination by a municipal coroner did not provided any clues towards the cause of death. Therefore, a formal assessment of causality cannot be made.

Other non-fatal serious cases. Ten other, non-fatal cases fulfill CIOMS criteria for seriousness, most of them because of hospitalizations. In some of them there were new events, and others had exacerbations of pre-existing conditions. Children were affected in three cases.
A 23-year old female, with an allergy to chicken egg protein, experienced symptoms suspect for a serious allergic reaction (angioedema, a generalised urticarial rash and presyncopic features). Due to a minutes latency, causality was assessed as probable (B).
One child was hospitalised due to an exacerbation of asthma, presenting one day after vaccination (C). Another child experienced a worsening of pre-existing epilepsy, attributed by the reporting parents to influenza vaccination (D).

A 77 year old man was hospitalised with macroscopic blood loss within 24 hours after vaccine administration. Causality cannot be excluded but it is more likely that the patient had asymptomatic thrombocytopenia already prior to vaccination (E).
A patient with breast cancer related surgery (many years earlier) experienced erysipelas after vaccination in the arm ipsilateral to the breast cancer, without specification whether lymph node resection was performed. Erysipelas occurred both after influenza vaccination in 2009 and 2010 (F).
One case concerns neurosarcoidosis presenting a few weeks after vaccine administration (G).

The group of remaining cases consists of a fulminantly presenting psoriasis in which an adverse drug reaction to a beta blocker was deemed most plausible by the reporting allergologist (H). Two cardiovascular events (TIA (I) and myocardial infarction (J)) were presented. One previously vital elderly patient experienced a persisting disabling pain origination from the injection site, impairing her social activities. The pain presented within minutes after administration. A diagnosis could not be established (K).

Non-serious cases of special interest. Presentation of rheumatoid arthritis, days after vaccination (M), one case in which a patient mentions exacerbations of rheumatoid arthritis associated with previous influenza vaccinations since 2006 (N). Also generalised urticaria (O) and facial edema (P) exacerbation of multiple sclerosis P and a bullous toxicodermia (Q) have been reported.

Serious cases concerning 2009/2010 seasonal influenza vaccines. One report was received regarding the influenza vaccinations in the previous season 2009/2010. It consisted of Guillain Barré syndrome attributed by the reporting patient both to pandemic influenza (8 days prior to presentation vaccinated) and to the 2009/2010 seasonal influenza vaccine with a more plausible time interval of four weeks, hence causality was considered possible for the seasonal vaccine, but less likely for the pandemic vaccine (L).

Table 2 Serious and other events of interest

id	no	sex, yr	vac dat	interval	causal	ser	event
A	112229	m 62	13-11-10	12-36 u	n.a.	death	sudden unexpected, unexplained death
B	110626	f 23	15-10-10	5min	probable		angioedema, rash and presyncope in patient with Crohn's disease
C	116914	m 5	02-11-10	1 d	possible	hosp	exacerbation of asthma
D	110719	m 10	19-10-10	1 d	possible	hosp	increased frequency of preexisting epileptic seizures
E	112379	m 77	19-11-10	<24 h	unlikely	hosp	thrombocytopenia
F	112150	f 64	27-10-10	13 d	possible	hosp	erysipelas
G	120761	f 71	21-10-10	weeks	unlikely	hosp	neurosarcoidosis
H	112696	m 75	09-11-10	1 d	possible	hosp	psoriasis
I	112157	f 78	6-11-10	1 d	n.a.	hosp	TIA brainstem with headache and hemiparesis recovering
J	111178	m 79	1-11-10	1 h	unlikely	hosp	myocardial infarction, life threatening, poorly documented
K	122025	f 72	02-11-10	0 d	possible	disab	disabling pain and atrophy injected arm
L	116270	m 66	4-11-09	4w	possible	hosp	Guillain-Barré syndrome. Patient also received pandemic influenza vaccine on 18-11-09
M	112108	f 57	22-10-10	2 d	unlikely		rheumatoid arthritis
N	118088	f 60	10-11-11	4 d	possible		aggravation of rheumatoid arthritis
O	112080	f 40	22-10-10	hrs	possible		urticarial rash episodes, hours and next evening
P	110781	f 51	19-10-10	hours	possible		exacerbation of preexisting multiple sclerosis
Q	110769	f 67	19-10-10	10 h	possible		fever, facial edema and malaise
R	117693	m 66	5-11-10	1 d	possible		bullous toxicodermia

(n.a.: causality not assessible)

5. Conclusions

Lareb received 146 reports of adverse events associated with administration of seasonal influenza vaccines, including one unexpected death of a recently vaccinated person. Due to the absence of any clues towards the cause of death, no formal causality assessment was possible. Ten other serious events were reported.
The events reported in the 2010/2011 season did not result in signals of unknown events with a plausible causality. The present findings are in line with the safety of seasonal influenza vaccination. The number of reports is low compared to the number of persons that has been vaccinated in the 2010/2011 season, especially when the morbidity of vaccinated persons is considered. More than 3,75 million doses of influenza vaccines have been administered. However, the number of reported events most probably represents a fraction of the true number of events due to underreporting.