Surveillance summaries

Supplementary report: surveillance of adverse events following immunisation among children aged less than seven years in Australia, 1 January to 30 June 2011

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Introduction

This report summarises national passive surveillance data reported to the Therapeutic Goods Administration (TGA) to 31 August 2011 for adverse events following immunisation (AEFI) reported for children aged less than 7 years who received vaccines between 1 January and 30 June 2011. The report includes all vaccines administered to children in this age group with a focus on the vaccines included in the funded National Immunisation Program (NIP) schedule.[1]

At the time of this report, the most recent change to the NIP schedule occurred in 2010 when annual seasonal trivalent influenza vaccine (TIV with 3 strains: A/H1N1, A/H3N2 and B) was funded for people aged ≥6 months with medical risk factors (previously subsidised through the Pharmaceutical Benefits Scheme).[2] A number of other important changes to vaccine funding and availability also occurred in 2009. From October 2009, the Northern Territory started using a new 10-valent pneumococcal conjugate vaccine (Synflorix®) at 2, 4, 6 and 12 months of age instead of the 3-dose 7-valent pneumococcal conjugate vaccine (Prevenar®) and a 23-valent pneumococcal polysaccharide booster for Indigenous children at 18 months of age. By late 2009, all states and territories were using the hexavalent DTPa-IPV-Hib-HepB (Infanrix hexa®) vaccine for all children at 2, 4 and 6 months of age,[3–5] due to an international shortage of PedvaxHib® (monovalent) and Comvax® (Hib-HepB) *Haemophilus influenzae* type b (Hib) vaccines.[6] To assist readers a glossary of the abbreviations of the vaccines referred to in this report is at the end of this report.

Methods

Case definition and coding

The data reported here are provisional only. It is important to note that an AEFI is defined as a medical event that is temporally, but not necessarily causally, associated with immunisation. Readers are referred to previous reports for a description of the national AEFI passive surveillance system,[7] methods used to analyse the data and information regarding limitations and interpretation of the data.[7–11] Often, several vaccines and reaction codes are listed in an AEFI record so the number of vaccines and reaction codes will exceed the total number of AEFI records. For the purpose of this report, an AEFI is defined as 'serious' if it is life-threatening, had recovery with sequelae, or was associated with admission to hospital, prolongation of hospitalisation, or death. In addition to the standard presentation of numbers and rates, in this report comparisons with previous years' data were made by whether reports included co-administration of influenza vaccines. This was done in order to facilitate comparisons with 2010 where there were a large number of AEFI reports for seasonal and pandemic influenza vaccines.

Denominator calculations from Australian Childhood Immunisation Register

Average annual population-based AEFI reporting rates were calculated using mid-2010 population estimates. Reporting rates per 100,000 doses were calculated for 10 vaccines on the NIP schedule for which reliable dosing data were available from the Australian Childhood Immunisation Register (ACIR), for children aged from birth to < 7 years.

Results

There was a total of 490 AEFI records (annualised reporting rate of 50.0 per 100,000 population) for vaccines administered to children aged < 7 years in the first 6 months of 2011. This was a 78% decrease on the 2,225 records (227.1 per 100,000 population) for the corresponding period in 2010. Forty-four (9%) were defined as 'serious' (i.e. recovery with sequelae, requiring hospitalisation, experiencing a life-threatening event or death). A total of 86 (18%) AEFI records were assigned a causality rating of 'certain' (n = 78, 16%) or 'probable' (n = 8, 2%). Thirty-four per cent (n = 167) of the 490 AEFI records for the 2011 reporting period were for children aged < 1 year; 13% (n = 66) for those aged 1 to < 2 years; and 52%

(n = 257) were for the 2 to < 7 year age group. The male to female ratio was 1.2: 1, which was similar to previous years.[8,9]

Eighty-seven per cent of AEFI (n = 427) were reported to TGA via states and territories and the remainder were reported direct to TGA: 9% (n = 46) by doctors or health care providers; 2% (n = 8) by hospitals; 1% (n = 4) by pharmaceutical companies; and 1% (n = 5) by members of the public. This is a sharp contrast to the same period in 2010 where 17% of cases were reported to TGA directly by members of the public, mainly because of the active promotion of the reporting of AEFI following the monovalent pandemic H1N1 influenza (pH1N1) vaccine directly to TGA, as well as a high level of public interest in both the pH1N1 and seasonal TIV vaccines.

Sixty-three reports listed one or more vaccines for which accurate dose denominator data were not available from the ACIR. These were influenza (n = 47), 23-valent pneumococcal polysaccharide (n = 7), Bacille Calmette-Guérin (n = 4), hepatitis B (n = 3), and hepatitis A (n = 2) vaccines. AEFI reporting rates per 100,000 doses were calculated for the remainder of records (n = 427) (Table).

Table: Reporting rates of adverse events following immunisation per 100,000 vaccine doses,* children aged less than 7 years, January to June 2011*

	Jan–Jun 2011			Reporting rate per 100,000 doses†*					
	AEFI records‡		Vaccine doses§	Jan–June 2011		Jan–June 2010		Jan–June 2009	
	n	n*	n	Rate	Rate*	Rate	Rate*	Rate	Rate*
Vaccine (NIP vaccines)‖									
DTPa-containing vaccines	332	331	529,539	63	63	37	32	44	44
DTPa-IPV	185	185	142,367	130	130	78	58	82	80
Pentavalent (DTPa-IPV-HepB)	0	0	103	0	0	NA		47	47
Hexavalent (DTPa-IPV-HepB-Hib)	147	146	387,069	38	38	23	22	30	30
Haemophilus influenzae type b	33	33	134,462	25	25	50	21	19	18
Haemophilus influenzae type b-hepatitis B	0	0	197	0	0	185	185	112	112
Measles-mumps-rubella	151	150	279,883	54	54	53	26	39	37
Meningococcal C conjugate	34	34	140,947	24	24	43	18	20	20
Pneumococcal conjugate	139	137	380,482	37	36	22	21	31	31
Varicella	30	30	133,815	22	22	58	14	9	9
Rotavirus	127	127	315,270	40	40	26	25	39	39
Age group									
< 1 year	161	160	1,028,266	16.0	16.0	10.0	9.0	13.0	13.0
1 to < 2 years	60	59	503,873	12.0	12.0	28.0	9.0	8.1	7.9
2 to < 7 years	206	205	309,905	67.0	66.0	42.0	30.0	41.0	40.0
AEFI category‖									
Total	427	424	1,842,044	23.0	23.0	20.0	12.0	17.0	16.0
'Certain' or 'probable' causality rating	74	74	1,842,044	4.0	4.0	1.2	1.4	2.5	2.5
'Serious' outcome	38	38	1,842,044	2.1	2.1	2.2	1.3	2.0	2.0

Source: Therapeutic Goods Administration database.

* Excludes any reports where 2010 seasonal TIV or pH1N1 were co-administered with the National Immunisation Program vaccines.

† Number of adverse events following immunisation (AEFI) records in which the vaccine was coded as 'suspected' of involvement in the reported adverse event and the vaccination was administered between 1 January and 30 June 2011. More than one vaccine may be coded as 'suspected' if several were administered at the same time.

‡ Records where at least one of the 10 vaccines shown in the table was suspected of involvement in the reported adverse event. AEFI category includes all records (i.e. total), those assigned 'certain' or 'probable' causality ratings, and those with outcomes defined as 'serious'. Causality ratings were assigned using the criteria described previously.[7] A 'serious' outcome is defined as recovery with sequelae, hospitalisation, life-threatening event or death.

§ Number of vaccine doses recorded on the Australian Childhood Immunisation Register (ACIR) and administered between 1 January and 30 June 2011.

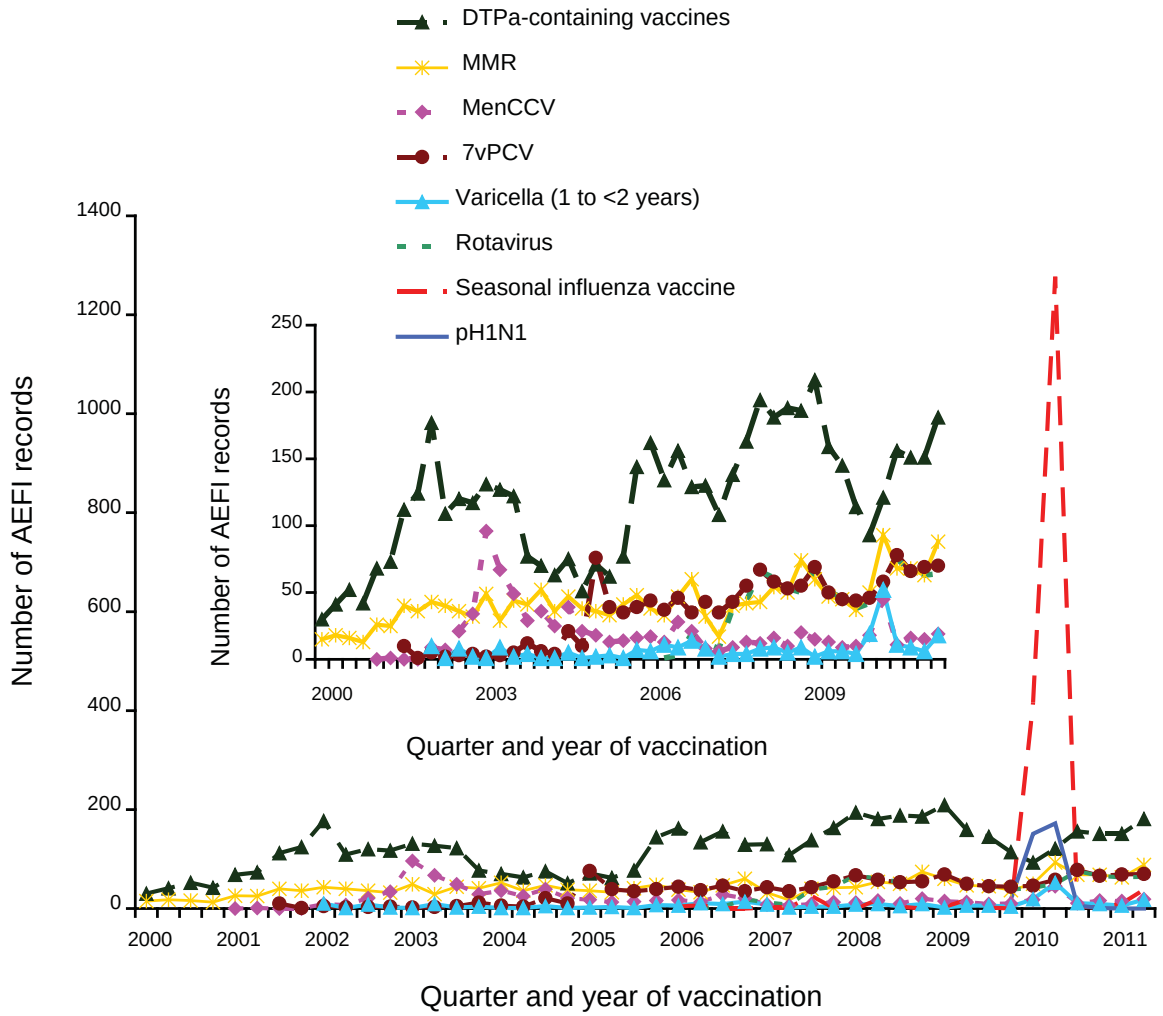
‖ The estimated AEFI reporting rate per 100,000 vaccine doses recorded on the ACIR.

NA Very few pentavalent (DTPa-IPV-HepB) doses.

The overall AEFI rate for those reports, for which accurate dosage data were available, was 23.2 per 100,000 doses, with 2.1 per 100,000 classified as 'serious'. Excluding any reports where seasonal TIV or pH1N1 were co-administered with other childhood vaccines made little difference to the reporting rates for 2011 (23.0 and 2.1), but they were higher than the corresponding rates for 2010 of 12.3 and 1.3, respectively. Reporting rates (excluding reports with influenza vaccine co-administration) were higher in 2011 for all age groups and vaccine types. The largest percentage increase in the AEFI reporting rates was observed for children aged 2 to <7 years (120%), followed by children aged <1 years (72%) and 1 to <2 years (30%). Increases were observed in reporting rates excluding any influenza-containing vaccines, following receipt of measles-mumps-rubella (MMR) (106%), DTPa-containing vaccines (98%), 7vPCV (69%), varicella (63%), and rotavirus (58%) (Figure). No AEFI reports for pentavalent (DTPa-IPV-HepB) and Hib-HepB during the period January to June 2010 were received; there were very few doses administered for these latter 2 vaccines.

The most commonly reported reaction categories were injection site reaction (ISR) (n = 202; 41%), fever (n = 133; 27%), allergic reactions (n = 89; 18%), rash (n = 56; 11%), gastroenteritis following rotavirus vaccination (n = 42; 9%), screaming (n = 33; 7%) and seizure (n = 20; 4%). The largest number of reports were from Victoria (41%) followed by Queensland (19%), New South Wales (13%), South Australia (11%), and Western Australia (9%). There were relatively more reports of ISR in 2011 compared with 2010 (189 in 2011 compared with 85 in 2010). In 2010, 31% reports

Figure: Reports of adverse events following immunisation, 1 January 2002 to 30 June 2011, for vaccines recently introduced into the funded National Immunisation Program*



Inset excludes pH1N1 and seasonal influenza vaccine.

* Meningococcal C conjugate vaccine (MenCCV) was introduced into the National Immunisation Program schedule on 1 January 2003; 7-valent pneumococcal conjugate vaccine (7vPCV) on 1 January 2005; DTPa-IPV and DTPa-IPV-HepB-Hib vaccines in November 2005; and Rotavirus (RotaTeq® and Rotarix®) vaccines 1 July 2007. In early 2008, Queensland, South Australia and Victoria changed from DTPa-IPV to DTPa-IPV-HepB-Hib for children at 2, 4 and 6 months of age.

were reported by Victoria followed by Queensland (28%), South Australia (13%) and New South Wales (10%). Compared with 2010, there was a substantial increase in reports of ISR in 2011 by all jurisdictions except the Australian Capital Territory and South Australia. The highest per cent increase was from Western Australia (200%), followed by Victoria and Queensland (180% each), the Northern Territory (170%), Tasmania (150%), and New South Wales (140%). A large number of ISR reports (n = 160; 85%) were from children aged 2 to < 7 years and 87% of these reports were associated with DTPa/IPV.

Nine per cent (n = 44) of the 490 AEFI records had outcomes defined as 'serious', however, there were no reports of life-threatening events, or deaths; all the children with AEFI defined as 'serious' were admitted to hospital. Thirty-four per cent (n = 15) of the 'serious' reports were following vaccination with hexavalent DTPa-IPV-HepB-Hib, 7vPCV, and rotavirus vaccines co-administered together. Serious and other significant AEFI included convulsions (n = 20 of which 6 were associated with hospitalisation), hypotonic-hyporesponsive episodes (HHE); (n = 19; 5 hospitalised), intussusception (n = 4; 3 hospitalised) and one case of idiopathic thrombocytopenic purpura (ITP). Of the 6 cases of seizure requiring hospitalisation, three were febrile convulsions (1 was following seasonal influenza vaccine while 2 others were following vaccination with varicella vaccine). There were a total of 14 reports of febrile convulsions; 43% were reported from Victoria. The most common individual vaccines in reports of convulsions were varicella (n = 5), seasonal influenza vaccine (n = 2), DTPa/HepB/IPV/Hib (n = 1), and DTPa/IPV (n = 1). The other reports of convulsions were following co-administration of Hib/MenC/MMR (n = 5), DTPa/HepB/IPV/Hib/7vPCV/rotavirus (n = 2), and one each of DTPa/HepB/IPV/Hib/7vPCV, 7vPCV/seasonal influenza, DTPa/IPV/MMR, and 23vPPV/HepA vaccines.

The majority of HHE (13/19) were notified by Victoria. Sixteen reports were following receipt of DTPa-containing vaccines, with hexavalent DTPa-IPV-HepB-Hib/ 7vPCV/rotavirus given conjointly in 15 reports and DTPa-IPV in one. Other vaccines in reports of HHE included Hib/MenC/MMR, Hib/MenC/varicella and rotavirus vaccine. Three of the 4 reports of intussusception in 2011 occurred following receipt of DTPa-IPV-HepB-Hib/7vPCV/rotavirus administered together and 1 report was following varicella vaccine. The only case of ITP was an infant following administration of Hib/MenC/MMR vaccine 18 days post-vaccination. There was no known medical history and the child fully recovered.

Discussion

There was a substantial decrease in the total number of AEFI records (78%) and population-based reporting rates (4.5 times lower) for the first 6 months of 2011 compared with the corresponding period in 2010. This appears to have been due to the drop in AEFI reporting following vaccination with seasonal TIV and pH1N1 influenza vaccines. The high number of reports associated with seasonal TIV and pH1N1 influenza vaccines in 2010 has been described previously.[8] High rates of fever and febrile convulsions were reported in association with one brand of the 2010 seasonal influenza vaccine used in children; this vaccine was withdrawn from use in young children from 2010.[12] The higher overall numbers of reports in 2011 (for non- influenza vaccines) is suggestive of generally increased propensity to report by providers in 2011, and may also reflect changes in the proportion of reports that were sent to TGA from individual state or territory surveillance systems. For example, in 2011, Victoria changed to submitting all reports to TGA, irrespective of severity, whereas previously minor/expected AEFI reports had not been submitted (personal communication: Dr Nigel Crawford, SAEFVIC, Victoria).

By age group, reporting rates per 100,000 doses, excluding vaccines co-administered with influenza, were higher in the first half of 2011 for all age groups, but more so in children aged 2 to < 7 years (66 vs 30) compared with children aged < 1 year (15.6 vs 9.0) and 1 to < 2 years (11.7 vs 9.0). The increase in reporting of AEFI in children aged 2 to < 7 years in 2011 was primarily because of increased reporting of ISR following vaccination with DTPa-IPV. The increase was largely seen from Victoria followed by Queensland and New South Wales.

The reporting rate of ISR in children aged 2 to < 7 years has declined in recent years, as was expected following the removal of the dose of DTPa-IPV due at 18 months of age from the NIP schedule in September 2003.[10] The reasons for the increase in 2011 are not entirely clear but at least partly due to general changes in AEFI surveillance stated above. One additional suggested hypothesis is that some ISR's are 'Arthus reactions' caused by the presence of high levels of prevaccination IgG antibody in the vaccinees, which have been associated with higher rates of ISR.[13,14] Possible causes of higher pre-vaccination antibody levels include immunity induced from natural infection in the pertussis epidemic from 2008, which was notable for high notification rates in pre-school aged children,[15] as well as the earlier age of administration of the pre-school DTPa-IPV booster since the change of eligibility rules for provider and parent incentive payments.[16]

Conclusion

The total number of AEFI reported in children aged < 7 years in the first half of 2011 was reduced by 78% compared with the same period in 2010 when a large number of reports were submitted in association with influenza vaccines. However, reporting rates for other vaccines were higher in all age groups in 2011, after excluding vaccines co-administered with influenza. This may reflect a greater propensity by vaccine providers to report in 2011 as well as changes in surveillance and reporting procedures at health departments at the jurisdictional level to report all minor events to TGA. This increase was greater in the 2 to < 7 year age group, particularly for ISR following receipt of DTPa-IPV. If a real increase in ISR incidence has occurred, one possible explanation is higher pre-vaccination antibody levels, due to the recent pertussis epidemic and possibly also earlier receipt of the pre-school booster.

The majority of AEFIs reported to the TGA were mild transient events and the data reported here are consistent with an overall high level of safety for vaccines included in the NIP schedule.

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Abbreviations of vaccine types

7vPCV	7-valent pneumococcal conjugate vaccine
23vPPV	23-valent pneumococcal polysaccharide vaccine
BCG	Bacille Calmette-Guérin (i.e. tuberculosis)
DTPa	diphtheria-tetanus-pertussis (acellular) – paediatric formulation
dTpa	diphtheria-tetanus-pertussis (acellular) – adolescent and adult formulation
DTPa-IPV	combined diphtheria-tetanus-pertussis (acellular) and inactivated poliovirus (quadrivalent)
DTPa-IPV-HepB	combined diphtheria-tetanus-pertussis (acellular), inactivated poliovirus and hepatitis B (pentavalent)
DTPa-IPV-HepB-Hib	combined diphtheria-tetanus-pertussis (acellular), inactivated poliovirus, hepatitis B and Haemophilus influenzae type b vaccine (hexavalent)
HepA	hepatitis A
HepB	hepatitis B
Hib	*Haemophilus influenzae* type b
IPV	inactivated poliovirus vaccine
MenCCV	meningococcal C conjugate vaccine
MMR	measles-mumps-rubella
pH1N1	pandemic H1N1 influenza 2009
TIV	seasonal trivalent influenza vaccine (with 3 strains: A/H1N1, A/H3N2 and B)