Supplementary report: surveillance of adverse events following immunisation among children aged less than seven years in Australia, 1 January to 30 June 2012

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Introduction

This report summarises national passive surveillance data reported to the Therapeutic Goods Administration (TGA) to 31 August 2012 for adverse events following immunisation (AEFI) for children aged <7 years who received vaccines between 1 January and 30 June 2012. 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]

Recent changes to the NIP have impacted on AEFI surveillance data presented in this report. On 1 July 2011, Prevenar® (7-valent pneumococcal conjugate vaccine, 7vPCV) was replaced with Prevenar 13® (13-valent pneumococcal conjugate vaccine, 13vPCV) for children at 2, 4 and 6 months and a 4th dose for medically at risk children at 12 months of age in all states and territories except the Northern Territory (which adopted 13vPCV from 1 October 2011).[2] In addition, children aged between 12 and 35 months who had completed a primary course with 7vPCV were eligible to receive a free supplementary dose of Prevenar 13® from 1 October 2011 to 30 September 2012. Also from 1 October 2011, the Northern Territory Government provided a free dose of Prevenar 13® at 18 months for children who had previously received a primary course of Synflorix® (10vPCV) or a mixed primary pneumococcal course with Synflorix® and Prevenar®.[3]

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, methods used to analyse the data and information regarding limitations and interpretation of the data.[4-9] Often several vaccines and reaction codes are listed in an AEFI record so that 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 if it was associated with admission to hospital, prolongation of hospitalisation, or death.

Denominator calculations

Average annual population-based AEFI reporting rates were calculated using mid-2011 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 from birth to age <7 years.

Results

There was a total of 484 AEFI records (annualised reporting rate of 47.9 per 100,000 population) for NIP and non-NIP vaccines administered to children aged <7 years in the first 6 months of 2012. This was lower than the corresponding period in 2011 (532 records; 52.7 per 100,000 population). Of the 484 records, 37 (8%) were events defined as being 'serious' i.e. recovery with sequelae, requiring hospitalisation, experiencing a life-threatening event or death. All AEFI records were assigned a causality rating. Eighteen percent (n=87) were rated as 'certain', 1% 'probable' (n=5), while the rest were 'possible'. Forty-one percent (n=200) of records were for children aged <1 year, 17% (n=81) for those aged 1 to < 2 years and 42% (n=203) were for the 2 to <7 year age group. The male to female ratio was 1.2:1, similar to previous years.[5,6]

Eighty-eight percent of AEFI (n=424) were reported to the TGA via states and territories. The remainder were reported directly to the TGA, 9% (n=42) by doctors/health care providers, 2% (n=8) by members of the public, 1% (n=7) by hospitals and 0.6% (n=3) by pharmaceutical companies.

Thirty-seven reports listed one or more vaccine(s) for which accurate dose denominator data (number of people who received the vaccine) were not available from the ACIR. These were influenza (n=24), bacille Calmette-Guérin (BCG) (n=7), hepatitis B (n=6), 23-valent pneumococcal polysaccharide

(n=4), and hepatitis A (n=2) vaccines. AEFI reporting rates per 100,000 doses were calculated for the remainder of records (n=447) (Table).

The overall AEFI rate for those reports for which accurate dose denominator data were available was 20.0 per 100,000 doses, with 1.5 per 100,000 classified as being 'serious' which is slightly lower than for the same period in 2011 (25 per 100,000 and serious 2.3 per 100,000 doses respectively). In 2012, reporting rates were similar to or lower than those in 2011 for all age groups and vaccine types (Table). There was a 28% reduction in reports for children aged 2 to <7 years, and no change in other age groups. There were substantial decreases in reported AEFI following receipt of *Haemophilus influenzae* type b vaccine (Hib) (39%); diphtheria tetanus acellular pertussis inactivated poliomyelitis (DTPa-IPV) (19%); measles mumps rubella (MMR) (18%); hexavalent (DTPa-IPV-HepB-Hib) (16%); meningococcal C conjugate (MenC) (15%); varicella (13%) and rotavirus (6%) (Figure). During 2012, pneumococcal conjugate vaccine was suspected of involvement in 180 events (173 for 13vPCV and 7 for 7vPCV) being for children aged <7 years with 15 coded as being serious, all for 13vPCV, consistent with vaccine usage i.e. with 13vPCV replacing 7vPCV in July 2011.

Table: Rates of AEFI per 100,000 vaccine doses, children aged less than 7 years, TGA database, January to June 2012

	Jan-Jun 2011		Reporting rate per 100,000 doses† (95% CI)	
	AEFI records* n	Vaccine doses§ n	Jan–June 2012	Jan–June 2011
Vaccine (NIP vaccines)‡				
DTPa-containing vaccines	333	582,301	57 (51.2-63.7)	68 (61.1-75.4)
DTPa-IPV	177	164,040	108 (92.6-125.0)	133 (114.5-153.1)
Pentavalent (DTPa-IPV-HepB)	1	95	NA*	0
Hexavalent (DTPa-IPV-HepB-Hib)	155	418,166	37 (31.5-43.4)	44 (37.8-51.3)
Haemophilus influenzae type b	24	141,139	17 (10.9-25.3)	28 (20.0-38.8)
Haemophilus influenzae type b-hepatitis B	0	127	0	0
Measles-mumps-rubella	139	309,159	45 (37.8-53.1)	55 (47.0-64.8)
Meningococcal C conjugate	33	148,609	22 (15.3-31.2)	26 (18.5-36.2)
Pneumococcal conjugate (7vPCV)	7	25,423	28 (11.1-56.7)	40 (34.1-47.1)
Pneumococcal conjugate (13vPCV)	173	495,731	35 (29.9-40.5)	NA
Varicella	29	144,068	20 (13.5-28.9)	23 (14.9-31.2)
Rotavirus	153	339,487	45 (38.2-52.8)	48 (40.9-56.5)
Age group				
<1 year	187	1,188,402	16 (13.6-18.2)	18 (15.6-20.9)
1 to <2 years	72	602,677	12 (9.3-15.0)	13 (9.8-16.2)
2 to <7 years	188	394,965	48 (41.0-54.9)	68 (59.5-78.3)
AEFI category‡				
Total	**447**	**2,186,044**	**20 (18.6-22.4)**	**25 (22.8-27.5)**
'Certain' or 'probable' causality rating	84	2,186,044	3.8 (3.1-4.8)	4.0 (3.3-5.3)
'Serious' outcome	33	2,186,044	1.5 (1.0-2.1)	2.3 (1.7-3.1)

* Number of 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 2012. More than one vaccine may be coded as 'suspected' if several were administered at the same time.

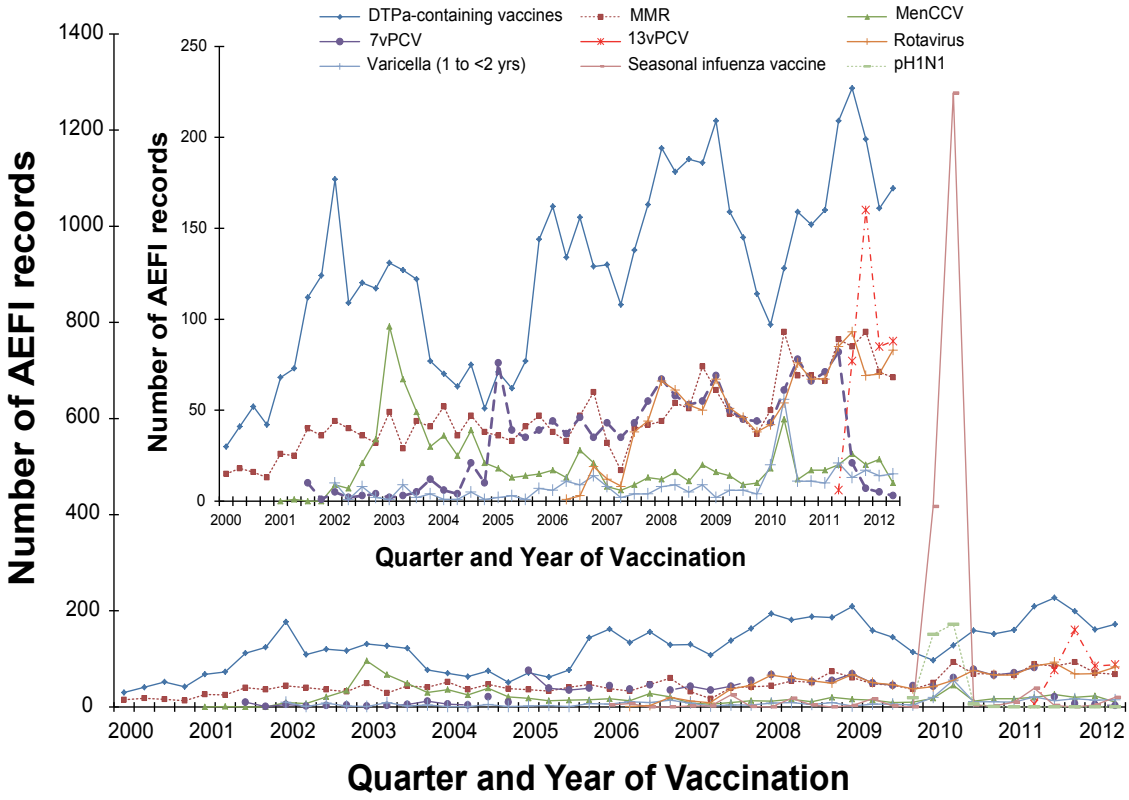
† The estimated AEFI reporting rate per 100,000 vaccine doses recorded on the ACIR.

‡ Records where at least one of the ten 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.[8] 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 2012.

NA Not applicable

Figure: Reports of AEFI, TGA database, 1 January 2000 to 30 June 2012, for vaccines recently introduced onto the NIP*



Inset excludes pH1N1 and seasonal influenza vaccine.

* Meningococcal C conjugate vaccine (MenCCV) was introduced into the NIP 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. pH1N1 influenza vaccine for children 6 months to 10 years on December 2009; seasonal trivalent influenza vaccine in 2010; and the 13-valent pneumococcal conjugate vaccine (13vPCV) on 1 July 2011.

The most commonly reported reaction categories were injection site reaction (ISR) (n=196;40%), fever (n=122;25%), allergic reactions (n=95;20%), rash (n=69;14%), gastroenteritis following rotavirus vaccination (n=55;11%), screaming (n=38;8%) and seizure (n=23;5%). The largest number of reports were from Victoria (41%) followed by Queensland (17%), Western Australia (15%), New South Wales (13%), and South Australia (7%).

Of the 196 reports of ISR, 85% were following DTPa-containing vaccines (73% with DTPa-IPV vaccine and 10% with hexavalent DTPa-IPV-HepB-Hib vaccine given either alone or conjointly with other vaccines). Seventy-six percent (n=149) of the reported ISR were from children aged 2 to <7 years and 95% (n=142) of those were following vaccination with DTPa-containing vaccines (139/142 were following vaccination with DTPa-IPV vaccine administered alone [37] or conjointly [102] with other vaccines).

Eight percent (n=37) of the 484 AEFI records had outcomes defined as being 'serious', a rate of 1.5 per 100,000 doses which was lower than the corresponding period in 2011 (2.3 per 100,000). There was one report of a life-threatening event and all the events in children (n=37) defined as being 'serious' were admitted to hospital, with no reported deaths.

The report of a life-threatening event was a premature infant who developed febrile seizures, encephalopathy and laryngospasm eight hours following vaccination with seasonal influenza vaccine (Fluvax®). The child inadvertently received the Fluvax® brand of influenza vaccine which has not been registered for use in <5 year olds since April 2010.[10]

Forty-one percent (n=15) of the 'serious' reports were following vaccination with hexavalent DTPa-IPV-HepB-Hib, 13vPCV, and rotavirus vaccines co-administered together. Serious and other significant AEFI included convulsions (n=23; 11 were serious of which 10 were hospitalised), hypotonic-hyporesponsive episodes (HHE, n=10; 3 hospitalised), intussusception (n=8; 5 hospitalised) and one case of idiopathic thrombocytopenic purpura (ITP) who was also hospitalised. Of the 10 cases of convulsions requiring hospitalisation, 7 were febrile convulsions. There were 15 reports of febrile convulsions in total. The most common vaccines given on their own cited in reports of convulsions were seasonal influenza vaccine (n=2),

DTPa-IPV (n=1), MMR (n=1), and varicella (n=1). The other reports of convulsions were following co-administration of hexavalent DTPa-IPV-HepB-Hib /13vPCV/rotavirus (n=5), Hib/MenC/MMR (n=3), DTPa-IPV/MMR (n=3), Hib/MenC/13vPCV/MMR (n=2), and one each of hexavalent DTPa-HepB/IPV-Hib-13vPCV-MenC, DTPa-IPV/MMR/varicella, HepB/MenC, HepB/Hib/MMR, and 23vPPV/Hep A/varicella vaccines.

Nine of the 10 reports of HHE were following receipt of DTPa-containing vaccines, with hexavalent DTPa-IPV-HepB-Hib/ 13vPCV/rotavirus given conjointly in 8 reports and hexavalent DTPa-IPV-HepB-Hib/ 7vPCV/rotavirus in one report. The report following non-DTPa vaccines were Hib/MenC/MMR.

There were 8 reports of intussusception in 2012; 6 occurred following receipt of hexavalent DTPa-IPV-HepB-Hib/13vPCV/rotavirus, one report hexavalent DTPa-IPV-HepB-Hib/7vPCV/rotavirus administered together while one report was following rotavirus vaccine administered alone.

The only case of ITP was an infant following administration of Hib/MenC/MMR vaccines 3 days post vaccination and was most likely due to MMR.

Discussion

There was a slight decrease in the total number of AEFI records and population-based reporting rates for the first six months of 2012 compared with the corresponding period in 2011.

Reporting rates per 100,000 doses for <1 year olds and 1 to <2 year olds were similar to the corresponding period in 2011, but significantly lower for children aged 2 to<7 years [48 (95% CI: 41.0 to 54.9) vs 68 (59.5 to 78.3)]. The decrease in reporting of AEFI in children aged 2 to <7 years in 2012 is primarily because of the drop in the reporting of ISR following vaccination with DTPa-IPV in that age group in 2012 compared to 2011. There was an increase in DTPa-IPV related ISR in 2 to <7 year olds in 2011 which might partly be due to general changes in AEFI surveillance nationally, discussed in a previous report.[5] Although reporting rates for DTPa-IPV vaccines were lower in 2012 compared to 2011, reporting was still higher than in previous years (78 in 2008; 82 in 2009; 78 in 2010) and therefore maintaining an upward trend.[6,7]

The increase in the reports following rotavirus vaccine may be because in the majority of the cases (86%), rotavirus vaccine was administered with 13vPCV and hexavalent vaccine. The chance of developing at least one AEFI with the administration of multiple vaccines is greater than with just one vaccine. Since October 2011, children aged between 12 and 35 months who had completed a primary pneumococcal vaccination course with 7vPCV have been eligible to receive a free supplementary dose of Prevenar 13®.[2] The increased AEFI reports following 13vPCV might be in part because it is being given as a 4th dose of PCV vaccine. Data from the clinical studies of Prevenar 13® demonstrated similar rates of injection site reactions when comparing 7vPCV with 13vPCV, with an increase following the 4th dose of either 7vPCV or 13vPCV in the second year of life compared with earlier doses in infancy. A similar trend was also observed for the other systemic reactions.[11] Some may also be attributed to the 'Weber effect',[12] which describes increased reporting frequently observed following the introduction of new vaccines.

Conclusion

The total number of AEFI reported in children aged <7 years in the first half of 2012 was lower than in the same period in 2011. Reports of ISR following DTPa-IPV at 4 years decreased in 2012 compared to 2011 but were still higher than in previous years. Reporting rates for most of the vaccines were similar to or lower in 2012, particularly in the 2 to <7 year age group.

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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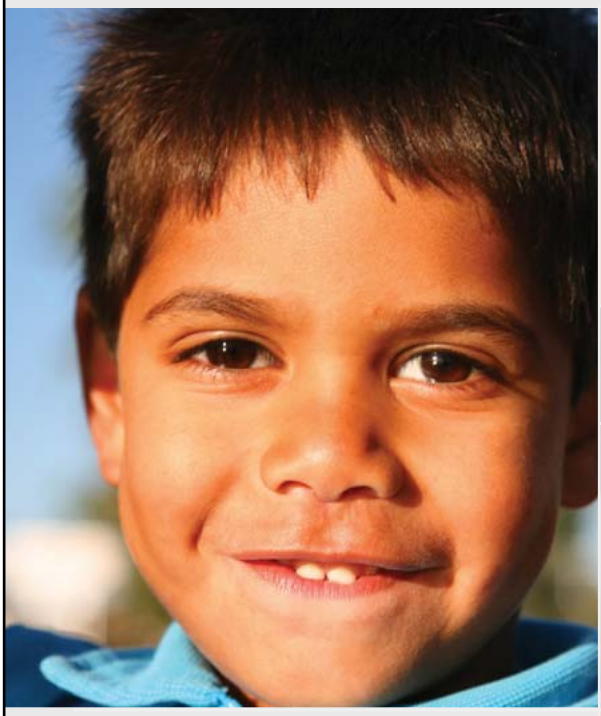

On the 28 March 2013, The Hon Tanya Plibersek MP, Minister for Health, launched the 10th edition of the Australian Immunisation Handbook.

Developed by the Australian Technical Advisory Group on Immunisation, and approved by the National Health Medical Research Council, the latest edition of the *Handbook* introduces new vaccines, contains new and updated recommendations on vaccine use and outlines the importance of vaccination during pregnancy.

New vaccines to the immunisation schedule include extending the Human Papillomavirus (HPV) vaccine to boys, the new combined MMRV vaccine, and a replacement pneumococcal vaccine.

The *Handbook* includes important information about catch-up vaccination schedules, vaccination for special risk groups, vaccination for groups with special requirements, and vaccination for international travel. An easy-to-read summary table is included which provides recommendations for vaccines during pregnancy. There is also information about managing rabies and Australian bat lyssavirus exposures.

In April 2013, copies of the *Handbook* were distributed to Australian immunisation providers including general practitioners, specialist doctors (e.g cardiologists, gerontologists, gynaecologists, obstetricians, oncologists and paediatricians), nurses, midwives, Aboriginal Health workers and travel clinics.

The *Handbook* has also been sent to hospitals, medical colleges, state and territory health units, Medicare Locals, National Aboriginal Community Controlled Health Organisations, Immunisation Committees, non-government organisations, pharmaceutical companies, migrant health services, health insurance companies, universities and libraries.

An electronic version of the *Handbook* is available on the Immunise Australia at www.immunise.health.gov.au. Copies of The *Handbook* can be ordered on the Immunisation Australia website - Publications & Resources.

Enquiries regarding the *Handbook* can be forwarded to handbook@health.gov.au

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