Surveillance summaries

Supplementary report: surveillance of adverse events following immunisation among children aged less than seven years in Australia, 1 January to 30 June 2009

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Introduction

This report summarises national passive surveillance data reported to the Therapeutic Goods Administration (TGA) to 31 August 2009 for adverse events following immunisation (AEFI) in children aged less than 7 years who received vaccines between 1 January and 30 June 2009. 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]

The most recent change to vaccine funding and availability that impacts on the AEFI surveillance data in this report compared with the same period in 2008 is the changeover to the single hexavalent DTPa-IPV-HepB-Hib vaccine for all children at 2, 4 and 6 months of age,[2–4] due to an international shortage of some *Haemophilus influenzae* type b (Hib) (PedvaxHib® [monovalent] and Comvax® [Hib-HepB] vaccines.[5] In March 2008, Queensland, South Australia and Victoria changed from using 2 combination vaccines (quadrivalent DTPa-IPV and Hib-HepB) to the single hexavalent DTPa-IPV-HepB-Hib vaccine. In February 2009, Western Australia stopped using PedvaxHib® for Indigenous children so that all children received the single hexavalent DTPa-IPV-HepB-Hib vaccine. The Northern Territory continued using Comvax® until October 2009, when it also changed to the hexavalent vaccine. All other jurisdictions had already been using the hexavalent vaccine since November 2005.

The data reported here are provisional only. It is important to note that an AEFI is defined as a medical event that is temporally associated with immunisation but not necessarily causally associated with immunisation. Readers are referred to previous reports for a description of the national AEFI passive surveillance system,[6] methods used to analyse the data and information regarding limitations and interpretation of the data.[6–9] 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 there is a code of life-threatening severity or an outcome code indicating recovery with sequelae, admission to hospital, prolongation of hospitalisation or death.

Average annual population-based AEFI reporting rates were calculated using mid-2008 population estimates. Reporting rates per 100,000 doses were calculated for vaccines on the NIP schedule for which reliable dosing data were available, for children aged from 2 months to < 7 years, using data from the Australian Childhood Immunisation Register (ACIR).

Results

There was a total of 305 AEFI records (annualised reporting rate of 32.0 per 100,000 population) for children aged < 7 years for vaccines administered in the first 6 months of 2009. This was an 18% decrease on the 374 records (39.2 per 100,000 population) for the corresponding period in 2008. Forty-four percent (n = 134) of the 305 AEFI records for the 2009 reporting period were for children aged < 1 year; 12% (n = 36) for those aged 1 to < 2 years; and 44% (n = 135) were for the 2 to < 7 year age group, similar to the age distribution in previous years.[7–10] The male to female ratio was 1.1:1, also similar to previous years.[7,9]

Of the 305 records, 24 listed one or more vaccines for which accurate dose information was not available. These were influenza (n = 10), 23-valent pneumococcal polysaccharide (n = 2), hepatitis A (n = 2), hepatitis B (n = 5), Inactivated poliomyelitis (IPV) (n = 1) and bacille Calmette-Guérin (n = 4) vaccines. AEFI reporting rates per 100,000 doses were calculated for the remainder of records (281) (Table). This was an overall AEFI reporting rate of 14.7 events per 100,000 doses recorded on the ACIR, lower than the rate for the corresponding period in 2008 (16.9 per 100,000 doses). Rates for all age groups

and reaction categories were lower in 2009 than for the same period in 2008 (Table). The age group with the largest reduction was children aged 2 to < 7 years (24%). Reporting rates for most vaccines were similar to, or lower than, those for the same period in 2008. There were substantial decreases in reported AEFI following receipt of diphtheria-tetanus-pertussis (DTP)-containing vaccines (12%), rotavirus (11%) and varicella (54%) vaccines. There were increases in reports following meningococcal C (20%), measles-mumps-rubella (7%) and pentavalent (DTPa-IPV-HepB) and Hib-HepB, although the total number of reports and doses administered for these latter 2 vaccines were small.

Twelve per cent (n = 37) of the 305 AEFI records had outcomes defined as 'serious' (i.e. recovery with sequelae, or hospitalisation, or life-threatening event or death), a rate of 1.8 per 100,000 doses, and lower than for the corresponding period in 2008 (2.3 per 100,000 doses). There was 1 report of life-threatening event and another 36 children were admitted to hospital. The only report of life-threatening event was apnoea, bradycardia and seizures in an infant born prematurely at 29 weeks, which followed the first vaccination with hexavalent DTPa-IPV-HepB-Hib, 7vPCV, and rotavirus vaccines at 38 weeks of age. The infant was receiving medication for apnoea of prematurity at the time of vaccination. Seizures and apnoea are listed in the product information for hexavalent DTPa-IPV-HepB-Hib and 7vPCV but not for rotavirus vaccine. Serious and other significant AEFIs reported included hypotonic-hyporesponsive episodes (HHE) (n = 17 of which 4 were associated with hospitalisation), seizures (n = 12), intussusception (n = 4) and anaphylaxis (n = 1). For the first 6 months of 2009, the overall reporting rate was the same as in 2008 for HHE in

Table: Reporting rates of adverse events following immunisation (AEFI) per 100,000 vaccine doses,* children aged less than 7 years, Therapeutic Goods Administration database, 1 January to 30 June 2009

	AEFI records‡ (n)	Vaccine doses* (n)	Reporting rate per 100,000 doses§		
			Jan–June 2009	Jan–June 2008	Jan–June 2007
Vaccine†					
DTPa-containing vaccines	212	533,490	39.7	45.1	29.2
DTPa-IPV	110	144,624	76.1	77.6	40.4
Pentavalent (DTPa-IPV-HepB)	3	6,450	46.5	11.2	42.0
Hexavalent (DTPa-IPV-HepB-Hib)	99	382,416	25.9	24.4	8.9
Haemophilus influenzae type b	23	129,697	17.7	17.4	18.0
Haemophilus influenzae type b-hepatitis B	3	3,586	83.7	40.6	24.9
Measles-mumps-rubella	98	277,992	35.3	33.1	17.8
Meningococcal C conjugate	26	138,678	18.7	15.6	9.2
Pneumococcal conjugate	106	390,026	27.2	28.4	17.9
Varicella	10	133,482	7.5	16.4	12.6
Rotavirus	102	306,024	33.3	37.2	50.9
Age group					
< 1 year	124	1,102,955	11.2	12.8	8.1
1 to < 2 years	35	491,792	7.1	7.4	5.2
2 to < 7 years	122	318,228	38.3	50.5	35.6
AEFI category†					
Total	281	1,912,975	14.7	16.9	11.9
'Certain' or 'probable' causality rating	43	1,912,975	2.2	5.1	4.2
'Serious' outcome	34	1,912,975	1.8	2.3	1.2

* Number of vaccine doses recorded on the Australian Childhood Immunisation Register (ACIR) and administered between 1 January and 30 June 2009.

† 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.[10] A 'serious' outcome is defined as recovery with sequelae, hospitalisation, life-threatening event or death.

‡ 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 2009. More than 1 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.

total (1.5 per 100,000 doses) and HHE following DTPa-IPV-HepB-Hib (3.2 per 100,000 doses in 2009 versus 3.1 per 100,000 doses in 2008).

The most commonly reported reaction categories included injection site reaction (ISR) (n = 121; 40%), fever (n = 54; 18%), allergic reactions (n = 46; 15%), gastroenteritis following rotavirus vaccination (n = 37; 12%), rash (n = 34; 11%), screaming (n = 20; 7%) and seizure (n = 12; 4%), similar to the distribution in 2008.

Discussion

The total number of AEFI records and population-based reporting rates was 18% lower for the first 6 months of 2009 compared with the corresponding period in 2008. This reduction appears to be due to a combination of several factors. Firstly, approximately 4% fewer vaccine doses were administered in the 1st half of 2009 compared with 2008 due to the more widespread use of hexavalent vaccine for primary schedule doses across Australia. When expressed as a reported AEFI rate per 100,000 doses, the difference was less marked, being 12% lower in 2009 than in 2008. Secondly, reporting delay is likely to account for a level of under-estimation in the latest period (2009) similar to that seen in 2008 and 2007 of between 5% and 20%,[7,9] which would result in upwards revision for the final report. Thirdly, it is also likely that the decline in reports for infants is at least partly due to a stabilisation following the expected initial peak following the introduction of the rotavirus vaccine in 2007 (Figure). Unlike recent reports, there have been no known changes in surveillance systems expected to impact on this period.

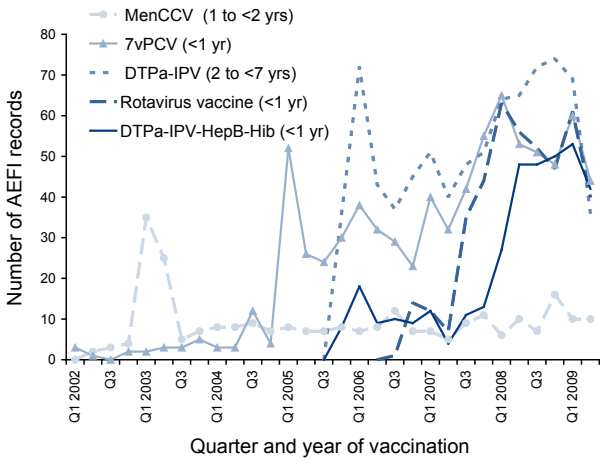
The increase in reporting rates for pentavalent DTPa and Hib-HepB should be interpreted with caution as the total number of doses administered and reported AEFI were low.

The episode of apnoea and reporting trends of HHE are deserving of further comment. Apnoea following immunisation in an infant born prematurely is a well recognised occurrence, which is usually self-limiting.[1] Trends in reporting HHE among children aged < 1 year are of particular interest. The reporting of HHE following receipt of hexavalent vaccine during the 1st half of 2009 (3.2 per 100,000 doses) was similar to that in 2008 (3.1 per 100,000 doses), after an increase from 0.5 per 100,000 doses in 2007 which has been attributed to changes in surveillance methods in Victoria.[11,12]

The observed reduction in the reporting rate for children aged 2 to < 7 years in 2009 compared with 2008 (38.3 and 50.5 per 100,000 doses, respectively) is primarily related to a reduction in ISR following acellular pertussis-containing vaccines. This AEFI is known to be very common among children receiving a 4th and 5th dose of acellular pertussis-containing vaccine.[6,8,13,14] The reporting rate of ISR in this age group declined in recent years (48 per 100,000 doses in 2007 compared with 78 per 100,000 doses in 2006), as was expected following the removal of the dose due at 18 months of age from the NIP schedule in September 2003. The reasons for the peak in 2008 and subsequent decrease are not entirely clear and may be at least partly due to changes in the propensity of general practitioners and others to notify adverse events and to reporting delays.

As discussed in previous reports, intussusception was associated with a previous rotavirus vaccine released only in the United States of America (USA) in 1998, and withdrawn from the market after 8 months.[15,16] All new generation rotavirus vaccines were closely monitored for intussusception during clinical trials and no association has been identified between the vaccines and intussusception.[17,18] Post-marketing surveillance for intussusception in association with vaccination continues internationally and, in Australia, through the Paediatric Active Enhanced Disease Surveillance pilot project. The 4 cases reported in the 1st half of 2009 is less than the number reported for the same period in 2008 (n = 11). The reporting rate in Australia in 2008 was found to be similar to that in the USA.[7]

Figure: Reports of adverse events following immunisation, Therapeutic Goods Administration database, 1 January 2002 to 30 June 2009, for vaccines recently introduced into the funded National Immunisation Program*



* 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.

Conclusion

In the first half of 2009 the AEFI reporting rate per 100,000 doses was 12% lower than for the same period in 2008. This appears to be attributable to a stabilisation of reports after the initial peak at the commencement of the rotavirus vaccination program in 2007, fewer reports of injection site reactions following pertussis-containing vaccines and perhaps also reporting delay. 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

DTPa	diphtheria-tetanus-pertussis (acellular) – paediatric 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)
HepB	hepatitis B
Hib	*Haemophilus influenzae* type b
Hib-HepB	combined *Haemophilus influenzae* type b and hepatitis B
IPV	inactivated poliovirus vaccine
7vPCV	7-valent pneumococcal conjugate vaccine