Surveillance summaries

Supplementary report: surveillance of adverse events following immunisation among children aged <7 years in Australia, 1 January to 30 June 2008

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Introduction

This report summarises national passive adverse events following immunisation (AEFI) surveillance data notified to the Therapeutic Goods Administration (TGA) at 30 September 2008 for children aged less than 7 years who received vaccines between 1 January and 30 June 2008. 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]

There were recent changes to both the AEFI surveillance system and funded immunisation program that influence the interpretation of AEFI data for vaccines administered to children aged <7 years during January to June in 2008 compared with the same reporting period in 2007 and previous years. During mid-2007 Victoria implemented an enhanced AEFI surveillance system across the state,[2] while a pilot project of enhanced hospital-based surveillance for selected AEFI commenced in 4 tertiary paediatric hospitals (in Sydney, Melbourne, Adelaide and Perth).[3]

Changes to the immunisation program occurred on 1 July 2007 when rotavirus vaccine[4] was added to the NIP schedule for all infants, and in March 2008 when, due to an international shortage of the Pedvax® and Comvax® formulations of *Haemophilus influenza* type b (Hib) vaccine,[5] 3 states changed from using 2 combination vaccines (i.e. DTPa-IPV and Hib-HepB) to the single hexavalent DTPa-IPV-Hib-HepB formulation for children at 2, 4 and 6 months of age.[6–9] This occurred in Queensland, South Australia, and Victoria. The hexavalent vaccine has been used in all other jurisdictions since November 2005 except for the Northern Territory, which uses a pentavalent DTPa-IPV-HepB and monovalent Hib vaccine for the infant immunisation schedule.

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,[10] methods used to analyse the data and information regarding limitations and interpretation of the data.[10–12] 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-2007 population estimates. Reporting rates per 100,000 doses were calculated for 10 vaccines on the NIP schedule using denominator data from the Australian Childhood Immunisation Register (ACIR).

Results

There was a total of 346 AEFI records (annualised reporting rate of 31.0 per 100,000 population) for children aged <7 years for vaccines administered in the first 6 months of 2008. This was a 32% increase on the 235 records (19.7 per 100,000 population) for the corresponding 6-month period in 2007 and the highest since 2003 when there were 485 AEFI records.

Forty-one per cent (n=143) of the 346 AEFI records for the 2008 reporting period were for children aged <1 year; 12% (n=40) for those aged 1 to <2 years; and 47% (n=163) were for the 2 to <7 year age group. Although there was an overall increase in the total number of AEFI records for the first 6 months of 2008, the distribution across age groups was similar to that seen in recent years.[11,13] The male to female ratio was 1.2:1, the same as the previous year.[11]

Twelve per cent (n=42) of the 346 AEFI records were defined as 'serious', slightly more than reported for the same period in 2007 (10%). Of the 42 serious AEFI records, one reported that the child had recovered with sequelae and 41 children were admitted to hospital. Serious and other significant AEFIs reported included anaphylaxis (n=1), seizure (n=14) and hypotonic-hyporesponsive episode (HHE; n=19)

Of the 346 AEFI records, 24 listed one or more vaccines where reporting rates could not be estimated from ACIR data due to some incomplete recording of doses on the ACIR. These were influenza (n=14), 23-valent pneumococcal polysaccharide (n=7), hepatitis A (n=4), combined hepatitis A-typhoid (n=1) and bacille Clamette-Guérin (n=1) vaccines.

AEFI reporting rates per 100,000 doses were calculated for 10 vaccines on the current NIP schedule for children aged 2 months or older (Table). These vaccines were recorded as suspected of involvement in the reported adverse event for 322 (93%) of the 346 records analysed. This is an overall AEFI reporting rate of 16.1 per 100,000 doses recorded on the ACIR with 2.0 'serious' AEFI records per 100,000 doses. AEFI reporting rates were higher than for the same period in 2007 and 2006 for most age groups,

Table. Reporting rates of adverse events following immunisation (AEFI) per 100,000 vaccine doses,* children aged less than 7 years, TGA database, January to June 2008

	AEFI records‡ (n)	Vaccine doses* (n)	Reporting rate per 100,000 doses§		
			Jan–June 2008	Jan–June 2007	Jan–June 2006
Vaccine†					
DTPa-containing vaccines	237	539,656	43.9	28.5	36.0
DTPa-IPV	165	212,159	77.8	39.1	46.2
Pentavalent (DTPa-IPV-HepB)	1	8,642	11.6	41.9	41.0
Hexavalent (DTPa-IPV-HepB-Hib)	71	318,855	22.3	8.8	16.8
Haemophilus influenzae type b	8	61,311	13.0	17.9	21.4
Haemophilus influenzae type b-hepatitis B	48	123,369	38.9	23.8	25.9
Measles-mumps-rubella	87	269,472	32.3	17.0	23.3
Meningococcal C conjugate	19	144,647	13.1	8.3	17.8
Pneumococcal conjugate	106	411,722	25.7	17.4	17.9
Varicella	20	131,775	15.2	15.3	15.8
Rotavirus	107	316,004	33.9	–	—
Age group					
<1 year	141	1,206,326	11.7	8.1	9.3
1 to <2 years	33	501,707	6.6	4.9	8.5
2 to <7 years	148	289,923	51.0	34.1	41.3
AEFI category†					
Total	322	1,997,956	16.1	11.7	15.1
'Certain' or 'probable' causality rating	104	1,997,956	5.2	4.2	6.2
'Serious' outcome	40	1,997,956	2.0	1.0	1.6

TGA Therapeutic Goods Administration

* Number of vaccine doses recorded on the Australian Childhood Immunisation Register (ACIR) and administered between 1 January and 30 June 2008.

† 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 2008. 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.

reaction categories and vaccines (Table), while the rates of AEFI with certain or probably causality ratings remained stable.

The largest changes were for children aged 2 to <7 years and <1 year, and for DTPa-IPV, hexavalent (DTPa-IPV-HepB-Hib), Hib-HepB and measles-mumps-rubella (MMR) vaccines. Observed changes in AEFI reporting rates for the first 3 vaccines were at least partly related to a large increase in the use of hexavalent vaccine and reduction in the use of DTPa-IPV and Hib-HepB vaccines in children aged <1 year in Queensland, South Australia and Victoria in early 2008 (see Introduction). The increase in AEFI reporting rates for children aged <1 year is also likely to relate to the implementation of the rotavirus immunisation program in July 2007. The vaccine is co-administered with 7-valent pneumococcal conjugate vaccine (7vPCV) and combination vaccines containing DTPa, IPV, Hib and HepB antigens.

One of the more significant AEFI reported for children aged <1 year is HHE. For the first 6 months of 2008, the reporting rate of HHE following DTPa-IPV containing vaccines plus co-administered vaccines was 9.9 per 100,000 doses of quadrivalent DTPa-IPV vaccine and 2.9 per 100,000 doses of hexavalent DTPa-IPV-HepB-Hib vaccine. While the reporting rate of HHE following DTPa-IPV vaccine was similar to that seen in 2007 (7.6 per 100,000 doses)[12] the rate following DTPa-IPV-HepB-Hib increased substantially in 2008 from 0.6 per 100,000 doses in 2007. The increase in reporting of HHE following DTPa-IPV-HepB-Hib and co-administered vaccines mainly occurred in Victoria, with little change for other states and territories (data not shown).

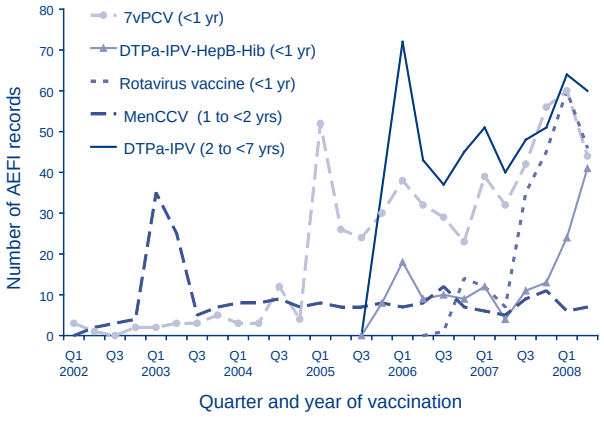
The very high reporting rate for DTPa-IPV vaccine of 77.8 per 100,000 doses (Table) includes reports for children aged <1 year (46.8 per 100,000) and children aged 2 to <7 years (98.6 per 100,000 doses). The majority of AEFI reports for the older age group listed injection site reaction (ISR; reporting rate of 92.7 per 100,000 doses). This is the highest reporting rate for ISR following DTPa-containing vaccines since 2002. The increase in the AEFI reporting rate for MMR vaccine in 2008 may relate to increased reporting of ISR following DTPa-IPV vaccine as the vaccines are administered at the same time in the 2 to <7 years age group and may have been administered in the same limb, or the actual injection sites not reported to the TGA.

Discussion

There was an increase in AEFI notified to the TGA for vaccines administered to children aged <7 years in the first 6 months of 2008 compared with the corresponding period in 2007, with the highest number of notifications since 2003. The majority of AEFI notifications described mild, transient and expected AEFI.

The increase in 2008 compared with the 2007 reporting period is likely to be due to several factors. There were fewer AEFI reports in 2007 compared with recent years, possibly related to there being no new vaccines added to the NIP schedule in the first 6 months of 2007 compared with 2005 and 2006.[11–13] Immunisation providers are more likely to report milder less serious AEFI for vaccines they are not familiar with. In Australia, it is evident that initial high levels of AEFI reporting occur each time a new vaccine is introduced into the NIP schedule, followed by a reduction and stabilisation of reporting over time (Figure). Corresponding peaks are also seen in reporting of co-administered vaccines (e.g. 7vPCV in Figure). The increase in AEFI reporting in 2008 appears to relate to an expected increase following the change to hexavalent vaccines in several jurisdictions in early 2008 as well as the introduction of the national infant rotavirus immunisation program in July 2007 (Figure). Major change in AEFI surveillance practices in Victoria where enhanced AEFI surveillance was implemented during 2007[2] has also

Figure. Reports of adverse events following immunisation, Therapeutic Goods Administration database, 1 January 2002 to 30 June 2008, for vaccines recently introduced into the funded National Immunisation Program*



* 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.

contributed to the increase in AEFI reporting for children aged <7 years for the first 6 months of 2008 compared with the same period in 2007.

Of particular interest are trends in reporting of ISR following acellular pertussis-containing vaccines among children aged 2 to <7 years and HHE among children aged <1 year. As noted previously,[12] the reporting rate of HHE following receipt of hexavalent DTPa-IPV-Hib-HepB has been lower than that following receipt of the antigens as 2 separate vaccines (i.e. DTPa-IPV and Hib-HepB). This may be related to a real difference in the occurrence of HHE following these 2 vaccines, or to surveillance factors. Interestingly, the significant increase in reporting of HHE following receipt of hexavalent vaccine in 2008, compared with 2007 (2.9 versus 0.6 per 100,000), suggests that surveillance is likely to play a major role as the increase mainly occurred for Victoria, which implemented a new AEFI surveillance system during 2007.[2,3] No increase was observed for Queensland or South Australia, which also changed to the hexavalent vaccine in early 2008.[7–9]

It is also unclear whether the observed rise in reporting of ISR following DTPa-IPV among children aged 2 to <7 years is related to changes in surveillance methods or a real increase in ISR, including extensive limb swelling. This AEFI is known to occur among children receiving a 4th and 5th dose of acellular pertussis-containing vaccine.[10,12,14,15] The reporting rate of ISR in this age group appeared to decline in recent years, as was expected following the removal from the NIP schedule in September 2003 of the dose due at 18 months of age. Children entering school in 2008 would have received their fourth dose of an acellular pertussis-containing vaccine at 4–5 years of age, whereas children in earlier birth cohorts would have received their 5th dose prior to school entry. Reporting of ISR following acellular pertussis-containing vaccines will continue to be monitored through the AEFI surveillance system.

Conclusion

This report further demonstrates that changes to the NIP schedule and to surveillance practices are reflected in the national passive AEFI surveillance data.[6,8,10] The majority of AEFI reported to the TGA were mild transient events and indicate the high safety level of the vaccines included in the NIP schedule. Close monitoring of passive AEFI surveillance data for vaccines administered to children continues through the TGA, in consultation with the Adverse Drug Reactions Advisory Committee and state and territory health departments.

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