Supplementary report: surveillance of adverse events following immunisation among children aged less than 7 years in Australia, 1 January to 30 June 2007

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Introduction

This report summarises national passive surveillance data collected by the Therapeutic Goods Administration (TGA) at 30 September 2007 for adverse events following immunisation (AEFI) reported for children aged less than 7 years who received vaccines between 1 January and 30 June 2007. 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 the NIP schedule occurred on 1 November 2005 with the addition of a single dose of varicella vaccine at 18 months of age, and the replacement of oral poliovirus vaccines with combination vaccines containing inactivated poliovirus (IPV) for doses due at 2, 4 and 6 months of age and 4 years of age. All children receive IPV in combination with diphtheria-tetanus-acellular pertussis (DTPa) antigens (i.e. DTPa-IPV).[1,2] For doses due at 2, 4 and 6 months, some states and territories use combination vaccines that include hepatitis B (HepB) virus antigens (i.e. DTPa-IPV-Hepb; pentavalent) or both HepB and *Haemophilus influenzae* type b (Hib) antigens (i.e. DTPa-IPV-Hepb-Hib; hexavalent). Rotavirus vaccines were added to the NIP schedule on 1 July 2007: after this reporting period. However, there has been a funded rotavirus immunisation program for infants in the Northern Territory from August 2006[3,4] (using Rotarix), and two rotavirus vaccines have been available on the private market to children elsewhere in Australia.[1,4]

Average annual population-based AEFI reporting rates were calculated using mid-2005 population estimates. Reporting rates per 100,000 doses were calculated for vaccines on the NIP schedule using denominator data from the Australian Childhood Immunisation Register (ACIR). Rates were not calculated for the birth dose of HepB due to inaccurate reporting of doses to the ACIR.

All AEFI reports received by the TGA are reviewed by the Adverse Drug Reactions Advisory Committee (ADRAC), an independent expert advisory committee to the TGA. 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[5] methods used to analyse the data and information regarding limitations and interpretation of the data.[5–7] Often, several vaccines and reaction codes are listed in an AEFI record so the number of both 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.

Results

All vaccines

There were a total of 176 AEFI records (annualised rate of 19.7 per 100,000 population) for children aged <7 years for vaccines administered in the first 6 months of 2007. This was a 34% decrease on the 266 records (29.8 per 100,000 population) for the corresponding six-month period in 2006. Thirty-eight per cent (n=66) of records were for children aged <1 year, 11% (n=19) for children aged 1 to <2 years and 52% (n=91) for children aged 2 to <7 years. This is similar to previous years,[6,8] except that there were fewer reports for children aged 1 to < 2 years in 2007. The male to female ratio was 1.2 to 1, the same as the previous year.[6]

Ten per cent (n=17) of the 176 records listed outcomes defined as 'serious' (i.e. recovery with sequelae, hospitalisation, life-threatening event or death). This was less than reported for the same period in 2006 (13.5%). For the first 6 months of 2007, there were no reports of death and all 17 children with 'serious' AEFIs were admitted to hospital. Serious and other significant AEFIs reported included anaphylaxis (1), severe allergic reactions involving the cardiovascular and/or respiratory systems (2) and seizure (3). There were 14 reports of hypotonic-hyporesponsive episode (HHE).

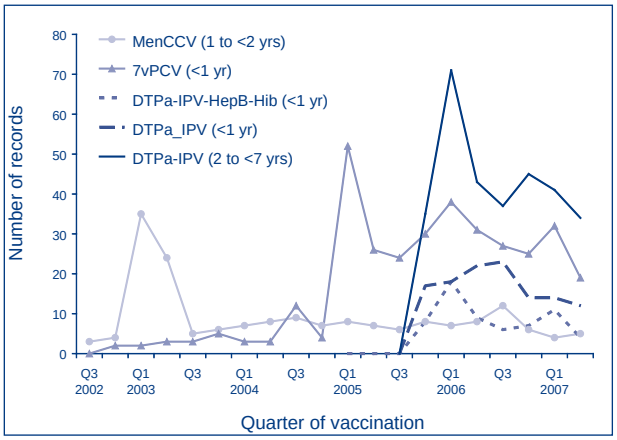
Of the 176 records, 13 listed one or more vaccines not included on the NIP schedule for children aged 2 months to <7 years as suspected of involvement in the reported AEFI. These were hepatitis B (n=2), influenza (n=3), and rotavirus (n=8) vaccines. There were a total of 14 reports for rotavirus vaccine including eight where it was the only suspected vaccine and six where NIP schedule vaccines were also listed as suspected of involvement in the reported AEFI. The most frequently reported signs listed in these 14 AEFI records were diarrhoea or vomiting (n=10) and fever (n=4).

National Immunisation Program schedule vaccines

One or more of the vaccines on the current NIP schedule for children aged 2 months or older were recorded as suspected of involvement in the reported adverse event for 163 of the 176 records analysed (Table). This is an AEFI reporting rate of 9.2 per 100,000 doses recorded on the ACIR with 1.0 per 100,000 doses defined as 'serious' AEFIs.

AEFI reporting rates per 100,000 vaccine doses were lower than for the same period in 2006 for all vaccines, age groups and reaction categories (Table). The largest reductions were for children aged 1 to <2 years and 2 to <7 years and for DTPa-containing vaccines, meningococcal C conjugate vaccine (MenCCV) and measles-mumps-rubella (MMR) vaccine. The reporting rate for AEFIs defined as 'serious' also decreased from 1.6 per 100,000 doses in 2006 to 1.0 per 100,000 doses in 2007. These changes appear to relate to a stabilisation of reporting to a baseline level after an initial increase following the introduction of multivalent IPV-containing vaccines in November 2005 (Figure), a reduction in the number of reports for the 1 to <2 year age group and a reduction in injection site reactions (ISR) following acellular pertussis containing vaccines at 4–5 years of age.

Reports of adverse events following immunisation, TGA database, 1 July 2002 to 30 June 2007, for vaccines recently introduced into the National Immunisation Program*



* Meningococcal C conjugate vaccine (MenCCV) was introduced into the NIP on 1 January 2003, 7-valent pneumococcal conjugate vaccine (7vPCV) on 1 January 2005, and DTPa-IPV and DTPa-IPV-HepB-Hib vaccines in November 2005.

Reporting rates of adverse events following immunisation (AEFI) per 100,000 vaccine doses,* children aged less than 7 years, Therapeutic Goods Administration database, January to June 2007

	AEFI records‡ (n)	Vaccine doses* (n)	Reporting rate per 100,000 doses§		
			Jan–June 2007	Jan–June 2006	Jan–June 2005
Vaccine†					
DTPa-containing vaccines	121	547,712	22.1	34.7	33.7
DTPa-IPV	101	345,564	29.3	44.2	–
Pentavalent (DTPa-IPV-HepB)	4	9,551	41.9	41.0	–
Hexavalent (DTPa-IPV-HepB-Hib)	16	192,597	8.3	16.8	–
Haemophilus influenzae type b	9	55,957	16.1	19.7	18.4
Haemophilus influenzae type b-hepatitis B	33	214,144	15.4	23.1	17.1
Measles-mumps-rubella	35	276,988	12.6	20.9	23.5
Meningococcal C conjugate	10	145,070	6.9	16.5	18.7
Pneumococcal conjugate	52	419,727	12.4	16.5	16.3
Varicella	14	131,065	10.7	13.3	–
Age group					
<1 year	56	990,723	5.7	8.6	6.2
1 to <2 years	19	488,695	3.4	7.5	7.5
2 to <7 years	88	311,245	28.3	38.7	25.4
AEFI category†					
Total	163	1,790,663	9.2	14.0	10.5
'Certain' or 'probable' causality rating	67	1,790,663	3.7	6.0	4.7
'Serious' outcome	17	1,790,663	1.0	1.6	0.6

* Number of vaccine doses recorded on the Australian Childhood Immunisation Register (ACIR) and administered between 1 January and 30 June 2007.

† Records where at least one of the nine 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.[5] 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 2007. 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 Australian Childhood Immunisation Register.

AEFI reporting rates for the different DTPa-IPV combination vaccines varied by age group and vaccine type (Table). The type of DTPa-IPV vaccine (i.e. quadrivalent, pentavalent, hexavalent) delivered to children aged <1 year varies by jurisdiction. The pentavalent vaccine is only used in the Northern Territory where children have also received rotavirus vaccine since August 2006.

The reporting rate for quadrivalent DTPa-IPV vaccine includes reports for children aged <1 year who were scheduled to receive the vaccine at 2, 4, and 6 months of age (reporting rate of 12.7 per 100,000 doses) and reports for children aged 2 to <7 years (reporting rate of 55 per 100,000 doses). This is the lowest reporting rate for acellular pertussis-containing vaccines for children in the 2 to <7 year age group since 2002. Previously, this had consistently been over 90 per 100,000, due mainly to a high level of reporting of ISR.[6,8] In the first 6 months of 2007, the rate of ISR for DTPa-IPV vaccine declined to 48 per 100,000 doses, compared with 71 per 100,000 doses for the same period in 2006, and an average of 78 per 100,000 doses of DTPa vaccine for 2002–2005.

Discussion

There was a large reduction in AEFI reports to the TGA for vaccines administered to children aged <7 years in the first 6 months of 2007 compared with the corresponding period in 2006. The most plausible explanation for the reduction relates to changes in reporting practices for all vaccines and age groups, plus a large reduction in reports for ISR following DTPa-containing vaccines

among children aged 2 to <7 years. There may also have been some delayed reporting of AEFI for immunisations administered between January and June 2007, although in the analysis, we have included AEFI reports received by the TGA up to 30 September 2007.

The passive AEFI surveillance system is sufficiently sensitive to be able to detect changes in reporting practices that are known to occur following the introduction of new vaccines. In Australia, it is evident that there are initial high levels of reporting each time a new vaccine is introduced into the NIP schedule, followed by a reduction and stabilisation of reporting over time (Figure, Table). This appears to have occurred in the January to June period of 2007 compared with the first 6 months of 2006, for the vaccines introduced into the NIP schedule in November 2005. Immunisation providers are more likely to report suspected less serious AEFIs for vaccines with which they are not familiar.

Of particular interest is the reduction in the ISR reporting rate for acellular pertussis-containing vaccines among children aged 2 to <7 years.[9] This may reflect a birth cohort effect related to the removal from the NIP schedule in September 2003 of the dose due at 18 months of age.[1,2] A large majority of children receiving a school entry dose of DTPa-IPV in the first 6 months of 2007 would have received three doses of acellular pertussis-containing vaccines due at 2, 4, and 6 months of age, and a fourth dose at 4–5 years. The rate of ISR has fallen by 38% from 78 per 100,000 doses to 48 per 100,000 in the first 6 months of 2007.[6,7] This suggests that the removal of the dose due at 18 months of age has had a significant impact on ISR reporting rates for acellular-pertussis containing vaccines in this age group.

Conclusion

This report further demonstrates that changes to the NIP schedule are reflected in the national passive AEFI surveillance data.[6,8,10] The majority of AEFIs 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 ADRAC and state and territory health departments.

Acknowledgements

We thank Mike Gold (ADRAC) and Peter McIntyre (NCIRS) for their contribution to this report. The National Centre for Immunisation Research and Surveillance is supported by the Australian Department of Health and Ageing, the New South Wales Health Department and the Children's Hospital at Westmead.

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