Australian Rotavirus Surveillance Program annual report, 2007/08

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Abstract

The National Rotavirus Reference Centre together with collaborating laboratories Australia-wide conducts a laboratory based rotavirus surveillance program. This report describes the types of rotavirus strains responsible for the hospitalisation of children with acute gastroenteritis during the period 1 July 2007 to 30 June 2008, the first complete year of surveillance following introduction of rotavirus into the National Immunisation Program. Six hundred faecal samples from across Australia were examined using a combined approach of monoclonal antibody immunoassays and reverse transcription-polymerase chain reaction. Of the 419 confirmed as rotavirus positive, serotype G1 was the dominant serotype nationally, representing 52% of specimens, followed by serotype G2 (19.8%), serotype G9 (12.2%), and serotype G3 (11%). No serotype G4 strains were identified. All G1, G3 and G9 strains assayed for P genotype contained the P[8] genotype, while all G2 strains contained the P[4] genotype, except one G2 strain which possessed a P[8]. Uncommon rotavirus genotypes, G8 (n=2) and P[9] (n=2) were identified during this study period. There was no evidence of unexpected changes in serotype distribution during the first 12 months of rotavirus vaccine use in the National Immunisation Program. *Commun Dis Intell* 2008;32:425–429.

Keywords: rotavirus, disease surveillance

Introduction

Rotavirus vaccine was introduced into the National Immunisation Program of Australia for all young infants from 1 July 2007. This is aimed to decrease the huge social and economic burden of rotavirus disease in Australia, which accounts for up to 50% of childhood hospitalisations for diarrhoea in Australia, and which represents 10,000 children hospitalised each year,[1] costing an estimated $30 million in direct costs.[2]

The 2 rotavirus vaccines, Rotarix® [GlaxoSmithKline] and RotaTeq® [Merck], have both been demonstrated to be safe and highly effective in the prevention of severe diarrhoea and hospitalisation due to rotavirus infections during large-scale phase III clinical and efficacy trials, each involving over 60,000 children worldwide.[3,4] In Australia, the state and territory health departments each made independent decisions on which vaccine to select; Victoria, South Australia, and Queensland selected RotaTeq®, while New South Wales, Western Australia, the Northern Territory, Tasmania and the Australian Capital Territory selected Rotarix®.

The Australian Rotavirus Surveillance Program has been reporting the changing annual pattern of dominant serotypes in the Australian population since 1999. Over this period our results highlight the diversity of rotavirus strains capable of causing disease in children, and provide the baseline information of the changing pattern of circulating strains, prior to vaccine introduction.[5–7]

The impact of these 2 widely used vaccines on the natural pattern of circulating rotavirus strains is unknown and difficult to predict, given the different components of each vaccine. Continuing serotype surveillance should identify the effects that each vaccine program has on circulating strains—in particular, whether changes occur in serotype incidence and whether increased proportions of rare or uncommon types result.

In this report we describe the surveillance and characterisation of rotavirus strains causing the annual epidemics of severe diarrhoea in young children in Australia for the period 1 July 2007 to 30 June 2008, the first 12 months in which rotavirus vaccine was available through the immunisation program.

Methods

Rotavirus positive specimens detected by enzyme immunoassay (EIA) or latex agglutination in collaborating laboratories were collected, stored frozen and forwarded to Melbourne together with relevant age and sex details. Specimens were then serotyped using an in-house monoclonal antibody (MAb) based serotyping EIA. The EIA employed a panel of MAbs specific for the major glycoprotein VP7 of the outer capsid of the 5 major group A human rotavirus serotypes (G1, G2, G3, G4 and G9).[8] Strains which could not be assigned a G serotype were genotyped by using a hemi-nested multiplex reverse transcription/polymerase chain reaction (RT-PCR), using G specific oligonucleotide primers.[9] P genotypes were determined by using a hemi-nested multiplex RT-PCR assay.[10]

Results

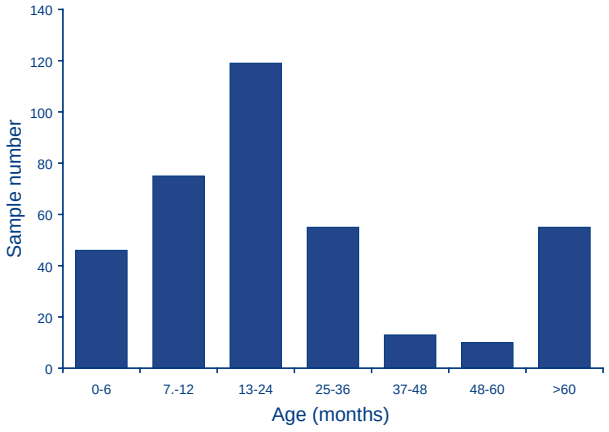
Number of isolates

A total of 600 specimens were received for analysis from Melbourne, Victoria and the collaborating centres in Western Australia, the Northern Territory, New South Wales and Queensland (Table). Specimens were not obtained from either South Australia or Tasmania. Four hundred and nineteen specimens were confirmed as rotavirus positive using our in-house EIA assay. The remaining 181 specimens contained either insufficient specimen for testing, or the specimens were not confirmed to be positive for rotavirus and were not analysed further.

Age distribution

The overall age distribution of children with acute rotavirus gastroenteritis is depicted in the Figure. In the reporting period, 11% of cases were from infants 0–6 months of age, 17.9% were from infants 7–12 months of age, 28.4% from patients 13–24 months of age, and 13.1% from patients 25–36 months of age. Overall, 86.9% of samples were from children aged 5 years or less.

Figure. Cases of rotavirus, Australia, 1 July 2007 to 30 June 2008, by age group



During the study period, slightly more specimens from male than female children (n=317 vs 247) were obtained for analysis.

Serotype distribution

The rotavirus serotypes identified in Australia from 1 July 2007 to 30 June 2008 are shown in the Table.

Table. Rotavirus G serotypes in Australia, 1 July 2007 to 30 June 2008

Centre	Total number	Serotype													
		G1		G2		G3		G4		G9		mix		NR	
		%	n	%	n	%	n	%	n	%	n	%	n	%	n
New South Wales															
Sydney (POW)	6	50	3	0.0	0	16.7	1	0.0	0	16.7	1	0.0	0	16.7	1
Sydney (Westmead)	33	39.4	13	27.3	9	21.2	7	0.0	0	0.0	0	3.0	1	9.1	3
Northern Territory															
Alice Springs	37	0.0	0	40.5	15	0.0	0	0.0	0	46	17	0.0	0	13.5	5
Darwin	18	0.0	0	61.1	11	11.1	2	0.0	0	22.2	4	0.0	0	5.6	1
Western Diagnostic (NT)	8	25	2	62.5	5	0.0	0	0.0	0	0.0	0	0.0	0	12.5	1
Queensland															
Brisbane	26	15.4	4	34.6	9	27.0	7	0.0	0	11.5	3	0.0	0	11.5	3*
Victoria															
Melbourne	82	64.6	53	5	6.1	18.3	15	0.0	0	3.7	3	0.0	0	7.3	6
Western Australia															
PathWest WA	134	68.7	92	11.2	15	3.7	5	0.0	0	11.9	16	0.0	0	4.5	5*
Perth	48	85.4	41	2.1	1	0.0	0	0.0	0	4.2	2	2.1	1	6.2	3
Western Darwin Pathology	27	0.0	0	48.2	13	33.3	9	0.0	0	18.5	5	0.0	0	0.0	0
Total	419	52.0	218	19.8	83	11.0	46	0.0	0	12.2	51	0.5	2	4.5	19

An additional 181 specimens were omitted from analysis due to insufficient sample or because the specimen was not confirmed to be rotavirus positive.

* Two samples were identified as genotype G8 (PerthWest and Brisbane).

Serotype G1 was the most common, representing 52% of all specimens, and was identified in Melbourne, Sydney, Perth and Brisbane, however only two of 90 rotaviruses identified in the Northern Territory were G1, both in Darwin. G1 was the dominant type in Melbourne, Sydney and Perth. Serotype G2 was the second most common type nationally, and represented 19.8% of specimens. It was identified in eight of the 10 collaborating centres and was the dominant type in Darwin and Brisbane. Strains belonging to serotype G9 were the third most common type identified, representing 12.2% of specimens. G9 was found in eight of the 10 centres, and was dominant in Alice Springs, prior to this surveillance period. This was probably related to the large rotavirus gastroenteritis outbreak which occurred in early 2007 in Alice Springs. Serotype G3 strains were identified in 7 centres during the study, and represented 11% of the total strains identified. No serotype G4 strains were identified in any centre. Two genotype G8 strains were identified during the study, one in Perth and one in Brisbane.

P genotype was determined for 116 of the rotavirus positive samples. All of the 25 G1 strains analysed were genotyped as P[8]. Similarly, all of the G3 and G9 strains analysed were also genotyped as P[8] (n=21 and 23, respectively). Thirty-eight of the 39 G2 strains analysed were associated with P[4]: 1 sample was typed as G2P[8]. Two G non-typeable strains were found to possess the P[9] VP4 gene.

Less than 0.5% of the rotavirus samples contained multiple serotypes. In 4.5% of the samples a serotype was not identified. The latter could be samples with virus numbers below the detection limits of our typing assays, or could have contained inhibitors in extracted RNA that prevent the function of the enzymes used in RT and/or PCR steps. Future studies will include further characterisation of the genes encoding the outer capsid proteins of these strains.

Faecal specimens were received from 12 children who developed gastroenteritis with 2 weeks of being vaccinated. No vaccine virus was identified in any of the cases, and in all cases wild type rotavirus strains were detected.

Discussion

In this report covering the period 1 July 2007 to 30 June 2008, we describe the annual epidemics and geographic distribution of the rotavirus types causing disease in Australian children during the first 12 months after national rotavirus vaccine introduction. Serotype G1 remained the dominant serotype nationally, comprising 52% of all strains characterised. It continues to be the dominant type on both sides of the country, in particular in Melbourne, Sydney and Perth, and was a minor strain in the Northern Territory. This survey continues to highlight the importance of serotype G1 as a major cause of disease in Australian children.

As noted in previous reports, multiple serotypes continue to co-circulate within the Australian population causing significant disease.[5–7] This year, G2, G3 and G9 were each identified in at least 7 locations during 2007–2008 and were all identified in greater than 10% of specimens.

The prevalence of G2 strains has increased during this survey, with G2 being the predominant type identified in the Northern Territory and Brisbane. During the 2004/05 and 2005/06 surveys G2 was a minor strain, identified in less than 2% of strains.[5,6] G2 has slowly increased in prevalence in Sydney and Melbourne, being the second most common strain during the 2006/07 period.[7] This year G2 predominated in the Northern Territory for the first time since it was responsible for a large outbreak of gastroenteritis in January 2004.[11]

In each of the G1, G3 and G9 strains analysed for VP4 genotype, the expected association with the P[8] VP4 protein was identified. Thus G1P[8], G3P[8] and G9P[8] combinations were the predominant strains identified in children during the current surveillance period similar to what is seen worldwide.[12,13] The G2 strains showed the expected association with the P[4] VP4 genotype, with 1 exception, the unusual G2P[8] strain that was identified in Brisbane. This is the first G2P[8] strain reported in Australia.

Both rotavirus vaccines used in Australia, RotaTeq and Rotarix have been shown to provide excellent protection against severe rotavirus gastroenteritis in large Phase III safety and efficacy trials.[2,3] RotaTeq® is a live attenuated bovine-human pentavalent vaccine. It contains rotavirus reassortants G1, G2, G3, G4 and P1[8] derived from rotaviruses infecting human and bovine species, which provides serotype specific protection against the most common rotavirus types. Rotarix® contains a live attenuated strain of human rotavirus (G1P[8]). Protection involves production of both specific and cross reactive antibodies, and has been demonstrated against serotypes G1, G3, G4 and G9. In a comparison of rotavirus types identified, based on vaccine usage in the various states, differences in the prevalence rates of G2, G3 and G9 were seen. G2 and G9 strains were more prevalent in states using Rotarix, whereas G3 strains were more prevalent in states using RotaTeq. These differences do not necessarily imply lack of protection by either vaccine against a particular type, but rather highlight the variation that can occur due to natural annual fluctuation in rotavirus strain prevalence.

Uncommon rotavirus types continue to be of worldwide interest because of the possible impact they may have on rotavirus vaccine programs. This year, 2 uncommon types have been identified in Australian children. Strains exhibiting a genotype G8 VP7 protein were identified in Perth and Brisbane, extending the previous identification of G8 in 2006–07 in Darwin. This continues the sporadic identification of G8 strains as a cause of acute gastroenteritis in Australian children.[7,14] The second uncommon type identified during this survey was the P[9] VP4 genotype in 2 strains. These strains were identified in Darwin, and represent the first report of P[9] in Australia. Previous reports of P[5] have been associated with G6 in the United States of America and Hungary, and G12 in Japan and Thailand.[12,13] Thus these reports of uncommon strains continue to highlight their low level existence in Australian children.

Prior to rotavirus vaccine introduction approximately 70% of clinical disease occurred among children less than 24 months of age.[7] During the previous survey (2006/07) 16% of faecal specimens were received from children admitted to hospital aged 0–6 months, and 23.9% of specimens were from infants aged 7–12 months. In comparison, the age distribution of children admitted to hospital during the first 12 months after implementation of the rotavirus vaccination programs has seen a slight reduction in the proportion of 0–6 and 7–12 month age groups affected, with 13% of specimens derived from infants aged 0–6 months, and 21% of specimens from infants aged 7–12 months. The potential impact of rotavirus vaccination is illustrated by the finding that no rotavirus positive specimens were received from infants aged 0–6 months in Darwin, despite faecal specimens being collected for serotype analysis from 54 children in Darwin during this survey period.

There have been no unexpected changes in the serotype distribution of rotavirus types causing disease in Australian children since the introduction of vaccination program nationwide. The rotavirus typing results from this survey, together with those of previous years, highlight the unpredictable nature of changes in the prevalence of rotavirus strains across Australia. In addition, the identification of rare or uncommon VP7 and VP4 genotypes further illustrate the diversity of strains capable of causing severe disease in Australian children. Understanding the fluctuations in rotavirus serotypes, using multicentre national surveillance, will provide valuable insight into vaccine efficacy over the next 3–5 years.

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