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Trends in rotavirus from 2001 to 2015 in two paediatric hospitals in Atlanta, Georgia

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Short Report

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Abstract

We compared rotavirus detection patterns before (2001–2006) and after (2008–2015) rotavirus vaccine introduction. We also compared rotavirus detection patterns in odd (2009, 2011, 2013, 2015) and even (2008, 2010, 2012, 2014) years post-vaccine separately. Results of stool rotavirus antigen testing from inpatient, outpatient and emergency department encounters from July 2000 to July 2015 at two paediatric hospital laboratories in Atlanta, Georgia were reviewed. Post-vaccine, rotavirus detection declined (30.2% *vs.* 13.7% (overall 54.6% decline, P <0.001)), occurred more frequently outside the rotavirus season (19.8% *vs.* 3.5%; $P < 0.001$), and was more common among older children (26 *vs.* 13 median months of age; $P < 0.001$). During odd years post-vaccine, rotavirus detection was significantly higher than even years (20.2% *vs.* 6.4%; $P < 0.001$). Rotavirus detection declined substantially and developed a biennial pattern in the post-vaccine era. The intensity and temporality of rotavirus detection in odd years post-vaccine resembled that observed pre-vaccine, although considerably reduced in magnitude.

Rotavirus vaccines, introduced in 2006 and 2008 in the USA, have reduced rotavirus-coded hospitalisations by 60–90% despite complete vaccination rates of only ~70% [1, 2]. Despite this reduction, rotavirus continues to cause gastroenteritis-related hospitalisations in about 5 per 10 000 children in the USA [3]. Before vaccine introduction, rotavirus had distinct winter–spring peaks of disease. Since 2008, peaks of rotavirus disease have occurred every other year, and seasons have been characterised by inconsistent timing and length [1]. We compared rotavirus detection patterns before (2001–2006) and after (2008–2015) rotavirus vaccine introduction using stool rotavirus antigen testing results from two children's hospitals in Atlanta, GA from 2001 to 2015. We also compared odd (2009, 2011, 2013, 2015) and even (2008, 2010, 2012, 2014) years post-vaccine separately.

Stool specimens were obtained for rotavirus testing from inpatient, outpatient and emergency department settings by physician order. Specimens were tested by SA Scientific RotaTest® (San Antonio, TX) from July 2000 to June 2006 and Remel Rotavirus Xpect® (Lenexa, KS) from July 2008 to July 2015. Tests that were duplicates (performed within 7 days), lacking basic information (e.g., results, date of birth) or from adults (>18 years of age) were excluded. All vaccine information was obtained from GRITS (Georgia Registry of Immunization Transactions and Services), a state vaccine registry.

Years were defined as Morbidity and Mortality Weekly Report (MMWR) week 27 (late June or early July) of the previous calendar year through MMWR week 26 of the stated year [4, 5]. We compared patterns of rotavirus detection in the pre-vaccine era (July 2000–June 2006) with those in the post-vaccine era (July 2007–July 2015). The year 2007 was considered transitional and excluded from analysis [4]. To assess a biennial pattern of rotavirus detection post-vaccine, odd (2009, 2011, 2013, 2015) and even (2008, 2010, 2012, 2014) seasons in the post-vaccine era were compared separately.

Rotavirus season onset and offset were defined as the first (or last) of two consecutive weeks in which at least two of ⩽10 stool specimens tested or at least 10% of ⩾11 specimens were positive [4, 6]. Rotavirus season peak was considered the week with the highest percentage of rotavirus detection.

All statistical analyses were performed using SAS 9.4 (Cary, NC), and statistical significance was assessed at the 95% confidence level. Medians and interquartile ranges (IQRs) were reported. Statistical comparisons were made between all the subgroups of interest using exact, non-parametric tests (exact Wilcoxon Rank-Sum or exact Kolmogorov–Smirnov) for continuous variables and Fisher's exact tests in discrete cases. This study was approved by the Emory University Institutional Review Board.

Differences observed between the pre- and post-vaccine eras

A total of 21 631 rotavirus test results were reported from July 2000 to July 2015. Of the 17 944 (83.0%) that were eligible for inclusion, 11 430 were obtained in the pre-vaccine era and 6514 were obtained in the post-vaccine era. Rotavirus detection among samples tested (30.2% *vs.* 13.7% (overall 54.6% decline, $P < 0.001$)) and rotavirus tests ordered (median 1948 *vs.* 763 tests per year (overall 60.8% decline, $P < 0.001$)) declined from the pre-vaccine to post-vaccine era (Supplementary materials). Rotavirus-positive children in the post-vaccine era were significantly older than those in the pre-vaccine era (26 (IQR 12–51) *vs.* 13 (IQR 8–22) median months; $P < 0.001$). A greater proportion of disease occurred among 24–36-month-old children post-vaccine than pre-vaccine (27.8% *vs.* 12.4%; $P < 0.001$).

A greater proportion of rotavirus detection occurred outside the season in the post-vaccine era compared with the pre-vaccine era (19.8% *vs.* 3.5%; $P < 0.001$). Although seasons tended to begin later (median MMWR week 5.0 *vs.* −0.5; $P = 0.281$), to peak later (median MMWR week 11 *vs.* 8.5; $P = 0.392$), and to be shorter (14.5 *vs.* 19.5 weeks; $P = 0.065$) in the post-vaccine era, none of these factors achieved statistical significance (Table 1).

Differences observed between the even and odd years in the post-vaccine era

Detection of rotavirus-positive children was higher in odd years post-vaccine than in even years (20.2% *vs.* 6.4%; $P < 0.001$) (Supplementary materials). Rotavirus-positive children were older in odd years post-vaccine than in even years (26 (IQR 12–52) *vs.* 22 (IQR 12–35) median months; $P = 0.03$). A delay in rotavirus season onset and shortening of seasons became more pronounced each even year, with no season occurring in 2014, but comparisons were not significant (Table 1). The detection of rotavirus remained approximately 6% in even years post-vaccine. A greater proportion of rotavirus disease occurred outside the rotavirus season in even years than in odd years (39.0% *vs.* 14.7%; $P < 0.001$).

Rotavirus detection declined substantially and developed a biennial pattern in the post-vaccine era. Rotavirus disease in odd years post-vaccine resembled that observed pre-vaccine, although considerably reduced in magnitude (20.2% *vs.* 30.2%). In even years, rotavirus detection declined to 6.4% (Table 1). We observed a trend towards delayed, shortened, blunted peaks of rotavirus disease beginning in 2009. In even years, a high proportion of detection occurred outside of the season (39.0%), and season onset and peak consistently occurred later until 2014 in which there was no defined season (Table 1). We did not find statistically significant evidence for rotavirus season shortening and delay; however, very small sample size, particularly in even years post-vaccine, limits conclusions regarding seasonality. National rotavirus surveillance data support the seasonality trends we observed in rotavirus detection post-vaccine [1, 7].

Post-vaccine, we recognised a 12-month increase in median age at the time of infection among rotavirus-positive children, with a greater proportion of 24–36-month-old children affected. The increased age of rotavirus-positive children, particularly pronounced in odd years, may be explained by the delayed age of infection in children temporarily shielded from rotavirus by indirect protection [8]. Since only ~70% of vaccine-eligible children in the USA are fully vaccinated against rotavirus, a sufficient population of rotavirus-susceptible children may accumulate every 2 years to amplify rotavirus transmission [1, 8]. Biennial surges in rotavirus disease have not been seen in countries with higher rotavirus vaccine coverage [9, 10]. Among rotavirus-positive children, the proportion of vaccine-eligible children vaccinated for rotavirus increased from 6% in 2008 to 40% in 2015 (Table 1). This increase in

Table 1. Summary of rotavirus seasonality and vaccination information in children tested for rotavirus from July 2000 to July 2015

Year[a]	# positive	# tested	% positive	% fully vaccinated[b]	% partially vaccinated[b]	Length of season: weeks	Onset: week	Offset week	Peak week
2001	398	1483	27	N.A.	N.A.	21	49 (−3)[c]	17	7
2002	485	1573	31	N.A.	N.A.	21	49 (−3)	17	8
2003	477	1883	25	N.A.	N.A.	18	3	20	11
2004	642	2085	31	N.A.	N.A.	17	1	17	9
2005	615	2012	31	N.A.	N.A.	18	7	24	12
2006	839	2394	35	N.A.	N.A.	25	50 (−2)	22	8
2008	87	1145	8	6	6	22	7	28	18
2009	180	1214	15	6	7	18	53 (0)	17	8
2010	45	812	6	13	10	13	8	20	19
2011	131	713	18	17	8	16	5	20	7
2012	27	492	6	29	10	4	17	20	19
2013	217	851	26	26	8	18	1	18	11
2014	36	612	6	42	0	0	None[d]	None	None
2015	169	675	25	40	13	12	2	13	7

[a]2007 was excluded as a transitional year.
[b]Among those that were rotavirus positive.
[c]Number assigned on an integer line based on MMWR week 52 as '0' for the purposes of calculating season length.
[d]None: 2014 did not meet rotavirus season criteria (as technically defined).

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rotavirus vaccine coverage among rotavirus-positive children is likely the result of an overall increase in rotavirus vaccine coverage since vaccine introduction in 2006. Inconsistency in rotavirus vaccine coverage from year to year may have limited our ability to compare rotavirus detection in odd *vs.* even years post-vaccine.

The notable decrease (60.8%) in the number of rotavirus tests ordered post-vaccine is an indicator of declines in rotavirus detection, but also may indicate less concern for rotavirus as a continued cause of paediatric gastroenteritis. Clinicians and clinical microbiologists should continue to be aware of rotavirus as an important cause of gastroenteritis and remain vigilant in testing, particularly during the winter and spring months of odd-numbered years. With the increased use of multiplex PCR panels for faecal testing in children's hospitals, physician-dependent, specific orders for rotavirus testing may become infrequent. Multiplex PCR may enhance detection of enteric viruses such as rotavirus; however, these highly sensitive assays may detect rotavirus from children with prolonged shedding after recent disease or vaccination, overestimating the true burden of disease [11].

This study is inherently limited by its retrospective, single-hospital design, reliance on physician-ordered testing and the paucity of outpatient data (<5%). Different assays were utilised between pre and post-vaccine eras but reported sensitivity and specificity for both are similar [12, 13]. Rotavirus genotyping was not available for this study.

A substantial, consistent reduction in rotavirus detection was observed after vaccine introduction. However, we observed biennial peaks of rotavirus detection post-vaccine with an increased proportion of detections occurring among 24–36-month-old children. Clinicians and clinical microbiologists should remain aware of rotavirus, particularly during the winter–spring months of odd years, and consider opportunities to increase use of rotavirus vaccines.

Supplementary material

The supplementary material for this article can be found at https://doi.org/10.1017/S0950268818000183

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