Impact of Rotavirus Vaccination on Hospital-Acquired Rotavirus Gastroenteritis in Children

WHAT'S KNOWN ON THIS SUBJECT: Approximately 27% of children with rotavirus in the hospital acquire it while hospitalized for another condition. Pediatric rotavirus vaccination greatly decreased the number of children hospitalized with rotavirus from 2007 to 2008.

WHAT THIS STUDY ADDS: Routine community-based rotavirus infant vaccination protects hospitalized children from acquiring rotavirus. Thus, community-based vaccination efforts should be encouraged as a strategy to decrease hospital-acquired rotavirus.

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abstract

OBJECTIVE: Data show that after the implementation of routine rotavirus vaccination for infants in the United States, community-acquired (CA) rotavirus cases declined substantially in the 2007–2008 season. The impact of community-based rotavirus vaccination on the substantial burden of hospital-acquired (HA) rotavirus has not been documented.

PATIENTS AND METHODS: We assessed CA and HA rotavirus, respiratory syncytial virus, and influenza infections at Children's Memorial Hospital for 5 winter seasons (defined as occurring from September through May) from 2003 to 2008. We also report rotavirus data from the 2008–2009 season.

RESULTS: A similar dramatic decline (>60% compared with the median of previous seasons) occurred in the rates of cases of both CA (P < .0001) rotavirus hospitalizations and HA (P < .01) rotavirus infections in the 2007–2008 season compared with previous seasons, whereas the rates of CA and HA influenza and respiratory syncytial virus, respectively, remained stable. Improvements in hand-hygiene compliance did not correlate with a reduction in the transmission rate of rotavirus in the hospital. Both CA and HA rotavirus rates remained much lower in the 2008–2009 than in the 2003–2007 seasons.

CONCLUSIONS: Community-based rotavirus vaccination is associated with a substantial reduction in the number of children who are admitted with rotavirus. These data also indicate that routine community-based rotavirus infant vaccination protects hospitalized children from acquiring rotavirus. Vaccination efforts should be encouraged as a strategy to affect the substantial burden of HA rotavirus. *Pediatrics* 2011;127:e264–e270

In the prevaccine era, rotavirus occurred in virtually all children by the age of 5 years, with ~1 in 80 US children requiring hospitalization.[1,2] Rotavirus primarily is transmitted fecal-orally, with hospital-acquired (HA) transmission occurring at rates of 0.46 to 15.8 per 1000 patient-days.[3–8] In the prevaccination era, an estimated 16 000 to 19 000 hospitalizations per year (~27% of the total rotavirus hospitalization burden) were because of HA rotavirus acquisition.[9] The first of 2 oral rotavirus vaccines was licensed in the United States in February 2006. During the 2007–2008 rotavirus season, a significant decline occurred in the rate of community-acquired (CA) rotavirus infections that temporally correlated with widespread rotavirus vaccination.[10–14] This dramatic decline was sustained into the 2008–2009 rotavirus season.[15] A decrease in the number of CA rotavirus hospitalizations could reduce the exposure of other hospitalized children to rotavirus, thus decreasing HA rotavirus. In this article, we describe the burden of HA rotavirus among pediatric inpatients at Children's Memorial Hospital (CMH) both before and after the introduction of rotavirus vaccination. We also compare HA rotavirus infections with 2 other common pediatric HA pathogens, influenza and respiratory syncytial virus (RSV), to help control for subtle changes in infection-control practices that could impact HA rotavirus.

PATIENTS AND METHODS

It was determined that this study be exempt from review by the CMH institutional review board. The study was conducted at CMH, a 270-bed pediatric hospital in Chicago, Illinois. Each winter viral season was defined as occurring from September 1 to May 31. During the winter viral season, all patients admitted with vomiting or diarrhea and all hospitalized patients with onset of vomiting or diarrhea underwent rapid antigen testing for rotavirus (X/pect Rotavirus [Remel, Lenexa, KS]) for infection control (bed placement). Similarly, all patients with fever and respiratory tract symptoms who required admission or hospitalized patients who developed these symptoms underwent rapid antigen testing for influenza (BinaxNOW Influenza A and B [Inverness Medical Professional Diagnostics, Princeton, NJ]) and RSV (BinaxNOW RSV [Inverness Medical Professional Diagnostics]). Infection-control staff met daily with charge nurses to discuss all hospitalized patients to ensure adherence to these policies. Contact precautions were used at CMH for patients with rotavirus, whereas contact and droplet precautions were used for patients with influenza or RSV.

HA rotavirus infections were defined as infections not present or incubating on admission with a positive test more than 72 hours after admission, whereas CA rotavirus infections were defined as infections with a positive test with symptoms on admission or 72 hours or less after admission. In addition, if rotavirus symptoms started less than 72 hours after hospital discharge and the patient was readmitted within 7 days of discharge with a positive rotavirus test, the infection was considered to be HA. A similar definition was used to differentiate HA from CA influenza, but for RSV the time was extended to 96 hours because virus incubation is longer.[16,17]

The number of CA and HA viral infections (rotavirus, influenza, and RSV), the number of hospitalizations, and the number of patient-days were determined for each viral season from September 1, 2003, to May 31, 2008. The number of CA viral infections per 100 hospital admissions and the HA viral infection rate per 1000 patient-days were calculated. A rate of transmission (HA cases and CA cases) was calculated to account for season-to-season variation in the burden of CA infections (which impacts the risk of HA infections). HA and CA rotavirus data were compared with those for influenza and RSV. In addition, health care worker hand-hygiene compliance rates during the viral season (assessed by independent observation) were available beginning September 2005 and were compared with transmission rates.

We also include CA and HA rotavirus data for 2008–2009. The occurrence of the influenza pandemic caused by the 2009 H1N1 influenza in the spring of 2009 substantially impacted the CA influenza numbers and also resulted in the implementation of a number of new infection-control policies that impacted the risk of HA influenza. Thus, only rotavirus data from 2008 to 2009 are presented.

Differences of the rates over time were compared using least-square means contrasts in the Poisson regression analysis. The linear regression analysis was conducted to evaluate the transmission rates of 3 viruses over time. Statistical significance was determined at the 5% level. Data were analyzed by using SAS 9.2 (SAS Institute, Inc, Cary, NC).

RESULTS

CA infections per 100 admissions are shown in Fig 1. The 2003–2004 season was relatively mild for both rotavirus and RSV. This was particularly the case for rotavirus when compared with the 2005–2006 ($P = .0211$) and 2006–2007 ($P = .0019$) seasons. In contrast, in 2003–2004 influenza had the highest admission rate compared with the following seasons: 2004–2005 ($P = .0001$); 2005–2006 ($P = .0003$); 2006–2007 ($P = .0376$); and 2007–2008 ($P = .0270$). CA rotavirus hospitalizations in the 2007–2008 season declined from
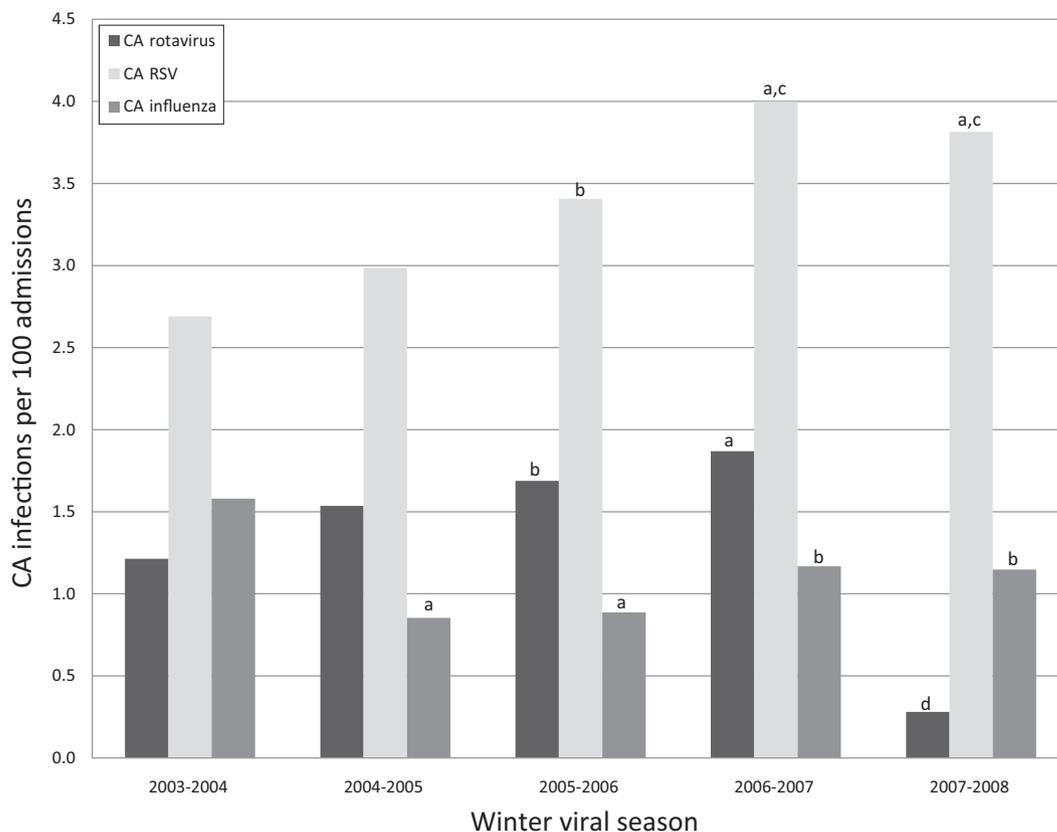
FIGURE 1

CA viral infection admissions per 100 admissions. [a] $P \leq .003$ versus the 2003–2004 season; [b] $P < .04$ versus the 2003–2004 season; [c] $P \leq .007$ versus the 2004–2005 season; [d] $P \leq .0001$ versus previous seasons. For exact P values, see the text.

1.62 per 100 admissions (a median rate of the 2003–2007 season) to 0.28 per 100 admissions ($P < .0001$ vs 2007–2008 to all previous seasons), an 82% decline in CA rotavirus admissions (Fig 1). In comparison, CA influenza and RSV admissions remained unchanged among neighboring seasons. The CA influenza rates only differed between the 2003–2004 and 2004–2005 seasons ($P = .0001$) but not other neighboring seasons (2004–2005 vs 2005–2006: $P = .8280$; 2005–2006 vs 2006–2007: $P = .0995$; and 2006–2007 vs 2007–2008: $P = .9051$). CA rotavirus admissions (0.53 per 100 admissions) in the 2008–2009 season remained lower than in the 2003–2007 seasons (all pairwise comparisons: $P < .0001$), but CA rotavirus admissions in the 2008–2009 season was higher than in the 2007–2008 season

($P = .018$ for comparison, data not shown in Fig 1).

HA infections per 1000 patient hospital-days are detailed in Fig 2. The 2006–2007 season was associated with a higher number of HA RSV infections compared with the 2003–2004 season ($P < .05$) and HA influenza infections compared with the 2004–2005 ($P = .0365$), 2005–2006 ($P = .0185$), and 2007–2008 ($P = .0091$) seasons. The median HA rotavirus rate was 0.53 per 1000 patient-days from 2003 to 2007. HA rotavirus infections in the 2007–2008 season declined to 0.20 per 1000 hospital-days (pairwise comparison P values: 2003–2004: $P = .0019$; 2004–2005: $P = .0049$; 2005–2006: $P = .0003$; and 2006–2007: $P = .0099$). HA rotavirus infections (0.10 per 1000 hospital-days) in 2008–2009 remained

much lower than the 2003–2007 seasons (pairwise comparison P values: 2003–2004: $P = .0004$; 2004–2005: $P = .001$; 2005–2006: $P < .0001$; and 2006–2007: $P = .0019$) and was not significantly different from 2007 to 2008 ($P = .4058$).

The rate of transmission (HA viral infections and CA viral infections) was not significantly different from 2003 to 2008 ($P = .6745$). The transmission rate for rotavirus (median 0.27 for 2003–2008) was almost 3 times greater than the rate of influenza ($P = .0045$) and was ∼6 times greater than the rate of RSV ($P = .0004$) transmission. The rates of transmission of influenza and RSV were not statistically significantly different ($P = .2158$) (Fig 3).

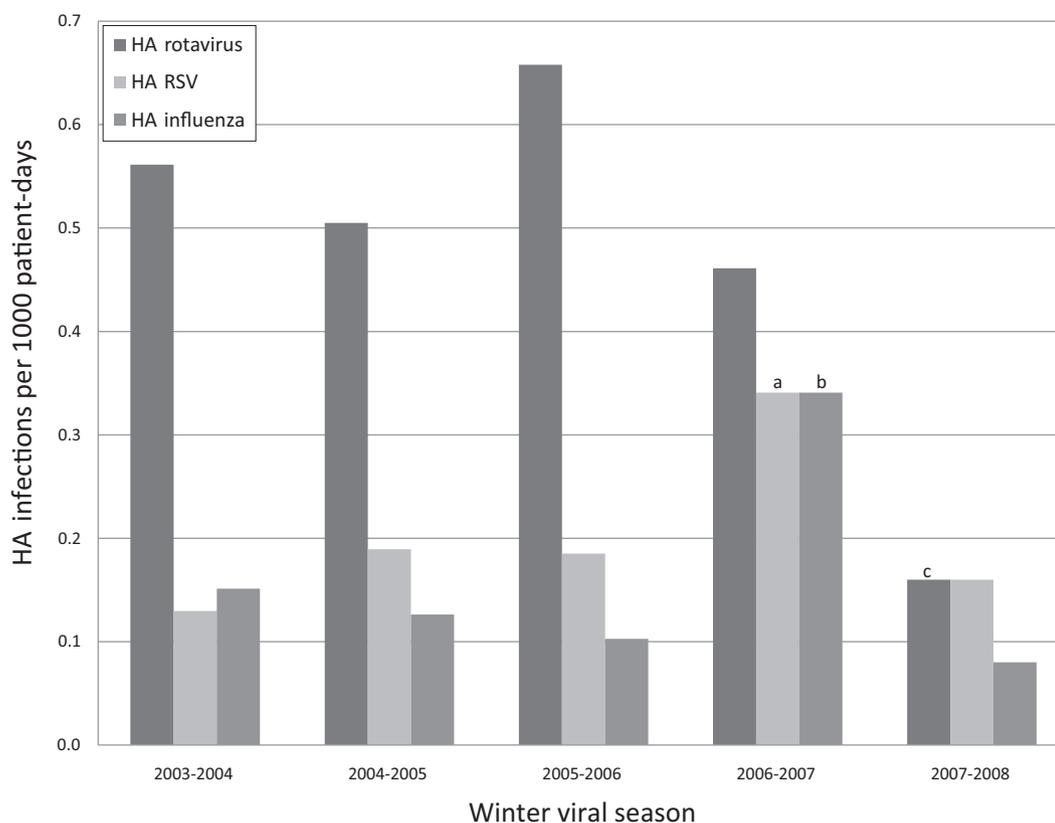Hand-hygiene compliance rates, as assessed by independent observation,

FIGURE 2
HA viral infections per 1 000 patient-days. [a] $P < .05$ versus the 2003–2004 season; [b] $P < .04$ versus the 2004–2005, 2005–2006, and 2007–2008 seasons; [c] $P < .01$ versus all previous years. For exact P values, see the text.

improved stepwise from 82.7% to 92.7% during the 4 winter seasons for which data (September 2005 through May 2009) were available. The improvement in hand-hygiene compliance did not correlate with a consistent improvement in the rates of transmission of any of these 3 pathogens.

DISCUSSION

In the 2007–2008 rotavirus season, we noted a 82% decline in CA rotavirus admissions from the previous median of the 2003–2007 season. These data mirror other published studies from the 2007–2008 season that noted a significant decrease (67%–87%) in CA rotavirus[10,11,13,18] and in all-cause acute gastroenteritis hospitalization rates.[14] Because only 31% of US children younger than 2 years old had completed 3 doses of vaccine, with single-

dose administration rates of 56% by the 2007–2008 season, this strongly suggests herd immunity.[10,13,19] In contrast, CA RSV and CA influenza hospital admission rates remained stable. The slight increase in CA rotavirus infections in the 2008–2009 season compared with the 2007–2008 season was similar to national data.[15]

Hospital acquisition of rotavirus infections occurs frequently. A recent review determined that roughly 27% of children hospitalized with rotavirus (16 000–19 000 hospitalizations per year) have acquired rotavirus infection while hospitalized for another condition.[9,20–22] This equates to transmission of rotavirus from 1 in every 3 children admitted with CA rotavirus to another hospitalized child. Similarly, we found that HA rotavirus accounted for ~19% of the total inpatient rotavi-

rus burden at CMH before 2007–2008. Potential reasons for the frequent transmission of rotavirus in the hospital include the large number of rotavirus virions shed in stool, the low rotavirus infectious dose, and prolonged shedding, which has been observed in hospitalized children.[2,23–25] One group concluded that because the percentage of rotavirus in the hospital that is HA has remained stable for 20 years, more stringent infection-control practices would not likely impact the burden of HA rotavirus.[22] Many groups have speculated that interventions that impact CA rotavirus hospital admissions (eg, vaccination) might also impact HA rotavirus rates.[3,6,7,9,21,22]

The substantial decline in CA rotavirus rates prompted us to evaluate whether HA rotavirus rates might be impacted as well. Coincident with the
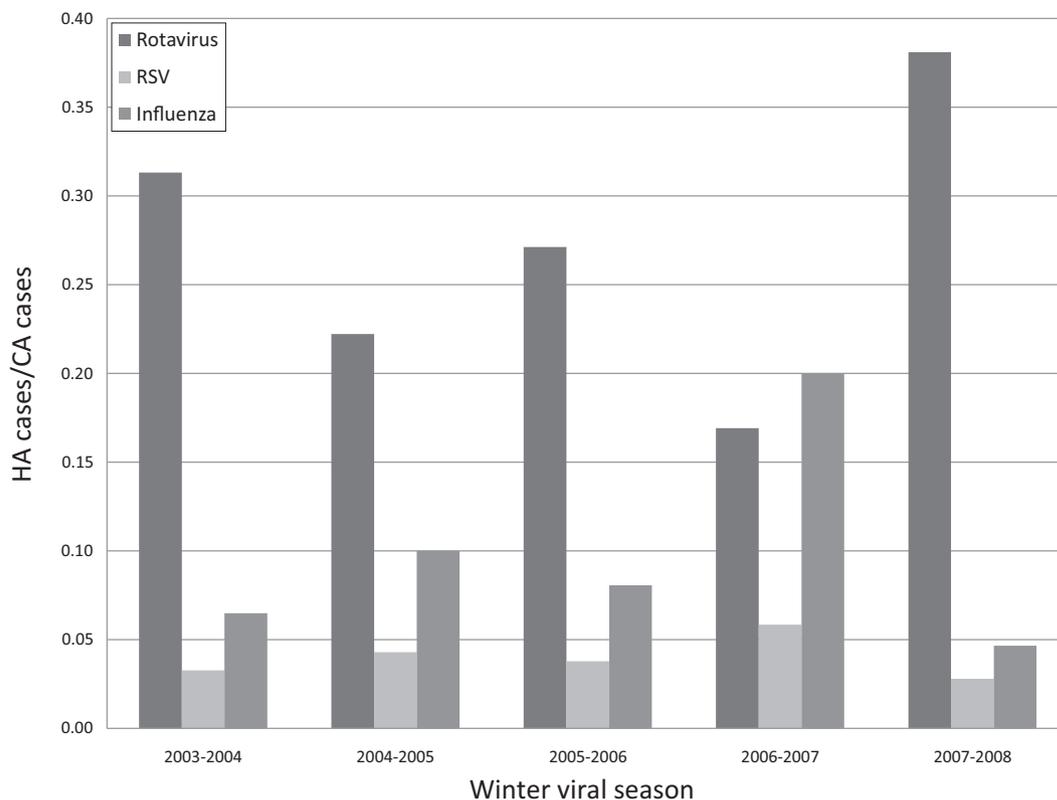
FIGURE 3
Viral transmission rate (HA cases/CA cases).

decrease in CA rotavirus rates, we documented a significant decrease in HA rotavirus rates in 2007–2008, in contrast with the stability of HA RSV and HA influenza rates. Potential reasons for this include fewer hospitalizations of children with CA rotavirus, resulting in less risk of transmission, and fewer hospitalized children may be at risk of rotavirus infection because of previous rotavirus vaccination. This study was unable to differentiate between these possibilities. Our data differ from those of children admitted to a pediatric hospital in Philadelphia, in which the absolute number of HA cases in 2007–2008 remained unchanged from 2005 to 2006.[11] The methods for identifying HA cases in that study were not detailed, and the reasons for differences in our results are not readily apparent.[11] The decrease in HA rotavirus rates we observed in 2007–2008 was sustained in 2008–2009.

To control for changes in infection control within the hospital and to control for changes in the year-to-year number of CA admissions, we also evaluated the rates of transmission (HA infections and CA infections) of rotavirus, RSV, and influenza. Thus, changes in infection control that lower the number of HA infections will result in a fall in the rate of transmission. The rate of transmission for rotavirus (median: 0.27 for the 2003–2008 seasons) remained unchanged and much higher than for influenza or RSV (Fig 3). Thus, for every 4 CA rotavirus hospital admissions, at least 1 child will acquire rotavirus while hospitalized for other reasons. Although we noted continued improvement in our independently observed hand-hygiene compliance, a corresponding decrease in the HA and CA rotavirus transmission rate did not occur. A potential explanation is that the 10% absolute increase in hand-hygiene compliance at CMH was insuf-

ficient to substantially impact HA rates. Our data confirm the opinion of others, which is that more stringent infection-control practices would be unlikely to impact the burden of HA rotavirus disease[22] and also confirm the hypothesis that vaccination, by impacting CA rotavirus hospital admissions, might decrease HA rotavirus rates.[3,6,7,9,21,22] Thus, community-based rotavirus vaccination efforts should be encouraged as a strategy for impacting the substantial burden of HA rotavirus.

One potential explanation for the decline in HA rotavirus rates would be a subtle unrecognized change in CMH's infection prevention and control efforts. Thus, we used other common pediatric viral pathogens (RSV and influenza) as comparators. Transmission of RSV occurs primarily by contact with contaminated secretions and via fomites with some transmission by

large particle droplets at short distances (<3 ft).[16] Thus, for both rotavirus and RSV, hand-hygiene and barrier precautions are considered crucial to prevention and containment.[17,26] Other groups[26–28] also have compared HA rotavirus and RSV and observed a similar burden of disease. Limited evidence exists that rotavirus also may undergo airborne transmission[9,20]; thus, influenza also was used as a comparator.[16] Rates of RSV and influenza transmission in our study were similar to rates observed in other studies.[29,30] The failure to observe any change in HA RSV and HA influenza rates in 2007–2008 strongly argues against a subtle unrecognized change in the methods of infection prevention and control as responsible for the decline in HA rotavirus rates.

Limitations of this study include the fact that these data are retrospective and from a single, large, tertiary care center. We may have missed hospitalized patients with mild gastroenteritis symptoms, but these patients likely would have been missed consistently each year.[21] It could be argued that the use of rapid antigen testing, particularly for influenza, resulted in the underdiagnosis of viral pathogens, because of the low sensitivity in clinical practice of the rapid antigen test.[31] This limitation, however, is unlikely to have impacted our conclusions because the same rapid antigen kits were used throughout the study and a symmetric underdetection of both CA and HA infections likely occurred. We also could not include data for RSV and influenza in 2008–2009 because of the onset of the pandemic 2009 H1N1 influenza that resulted in the implementation of many new infection-control strategies. The first of these measures occurred coincident with our last case of HA rotavirus in May 2009 and occurred after 75% of the CA rotavirus had occurred. Thus, it is unlikely that these efforts significantly impacted the risk of HA rotavirus. Because of our study design, we lack genotype data for the identified HA isolates, which would allow us to determine genetic relatedness of the HA isolates. We also were unable to assess the impact on hospital cost and severity of illness.

Important strengths of this study include the multiple years of baseline data from 2003 to 2007 and inclusion of comparison data from other common pediatric HA viral pathogens (RSV and influenza). These data provide the context in which to the substantial decline in both CA and HA rotavirus disease that began in 2007–2008.

CONCLUSIONS

These data provide strong supportive evidence for the impact of rotavirus vaccination on hospitalizations for CA rotavirus beginning in the 2007–2008 rotavirus season. The dramatic decrease in the number of CA rotavirus cases correlated with the decrease in HA rotavirus rates per 1000 patient-days in 2007–2008 that was sustained in 2008–2009. In contrast, rates of other common pediatric HA viral pathogens (RSV and influenza) remained stable. Improvements in hand-hygiene compliance did not seem to correlate with improvements in rates of transmission. Thus, community implementation of rotavirus vaccination dramatically decreases the substantial burden of HA rotavirus.

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