

First Reports of Human Rotavirus G8P[4] Gastroenteritis in the United States

Geoffrey A. Weinberg,^a Daniel C. Payne,^b Elizabeth N. Teel,^c Slavica Mijatovic-Rustempasic,^c Michael D. Bowen,^c Mary Wikswo,^b Jon R. Gentsch,^c and Umesh D. Parashar^b

Department of Pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, New York, USA,^a and Epidemiology Branch^b and Gastroenteritis and Respiratory Diseases Laboratory Branch,^c Division of Viral Diseases, National Center for Immunization & Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

In 2009, three children were hospitalized in Rochester, NY, with sequence-confirmed G8P[4] rotavirus gastroenteritis—the first U.S. detection of this uncommon strain more typically found in Africa. Continued monitoring of G8P[4] and other rotavirus genotypes not represented in current vaccines is essential to assess whether vaccination will result in an increase in prevalence of these strains.

CASE REPORTS

Case 1. In mid-April 2009, a 25-month-old girl was admitted to the Golisano Children's Hospital at University of Rochester Medical Center with a 3-day history of diarrhea and vomiting (12 to 20 episodes per day). Her maximum daily temperature was 38.3°C. She was previously healthy, although she was born prematurely after a 33-week gestation; she was breast-fed for the first 3 months of life. She lived in the Rochester, NY, metropolitan area and did not have any unusual animal, dietary, or travel exposures in the preceding 3 months. The child had not been vaccinated against rotavirus. Moderate dehydration and lethargy were noted upon physical examination; there were no other abnormalities. After intravenous rehydration in the hospital for 24 h, she was discharged to her home. At admission to the hospital, the child was enrolled, with parental informed consent, into an ongoing, active, prospective, population-based surveillance for acute gastroenteritis among children <5 years old (Centers for Disease Control and Prevention New Vaccine Surveillance Network [CDC NVSN]), the details of which have been previously published (23–26, 32). A stool sample taken during her hospitalization was positive for rotavirus antigen by enzyme immunoassay (Premier Rotaclone; Meridian Biosciences, Inc.). Her parents noted that one of her two siblings (each 3 to 4 years of age) experienced a few days of fever and emesis several days after the patient became ill, suggesting possible intrafamilial spread; however, no samples were taken from that child by their physician, and the sibling was not eligible for study enrollment. The patient's stool specimen was analyzed at the CDC by real-time reverse transcription-PCR (RT-PCR) genotyping and nucleotide sequencing of partial VP7 and VP4 genes as previously described (3, 14). BLAST searches of public databases using VP7 and VP4 sequences identified the strain as genotype G8P[4].

Case 2. In mid-April 2009, a 34-month-old girl was admitted to the Golisano Children's Hospital at University of Rochester Medical Center with a 5-day history of diarrhea and vomiting (3 to 10 episodes per day). Her maximum daily temperature was 37.7°C. She was previously healthy, born after a full-term gestation and breast-fed for the first 12 months of life. She lived in the Rochester, NY, metropolitan area and did not have any unusual animal, dietary, or travel exposures in the preceding 3 months.

TABLE 1 Characteristics of children with G8P[4] rotavirus acute gastroenteritis

Characteristic	Values for each case (strain)		
	1 (US09Ro103)	2 (US09Ro104)	3 (US09Ro045)
Age (mo)	24.8	33.5	53.5
Duration of symptoms at enrollment (days)	3	5	2
Maximum no. of daily episodes of diarrhea/maximum no. of daily episodes of vomiting	12/20	3/10	30/15
Length of hospital stay (days)	1	1	14 ^a
Previous rotavirus vaccination	None	None	None
Travel or contact with international travelers	None	None	None
Animal exposure	None	None	Horse
Unusual dietary exposures	None	None	None
Possible household spread ^b	Yes	Yes	No

^a Child subsequently diagnosed with inflammatory bowel disease (see text).

^b Based on parental report of illness.

The child had not been vaccinated against rotavirus. Moderate dehydration and lethargy were noted upon physical examination; there were no other abnormalities. After intravenous rehydration in the hospital for 24 h, she was discharged to her home. The child was enrolled into NVSN surveillance at admission. Stool testing was positive for rotavirus antigen by enzyme immunoassay, and subsequent partial VP7 and VP4 gene analysis at the CDC revealed that the isolate was genotype G8P[4]. Her parents noted that her 5-year-old sister became ill with diarrhea and vomiting 4 days after the patient's admission (and was herself admitted to the hospital for 3 days), suggesting possible intrafamilial spread; however, no samples were taken from this contact.

Case 3. During late March of 2009, a 54-month-old boy was

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Address correspondence to Geoffrey A. Weinberg, geoff_weinberg@urmc.rochester.edu.

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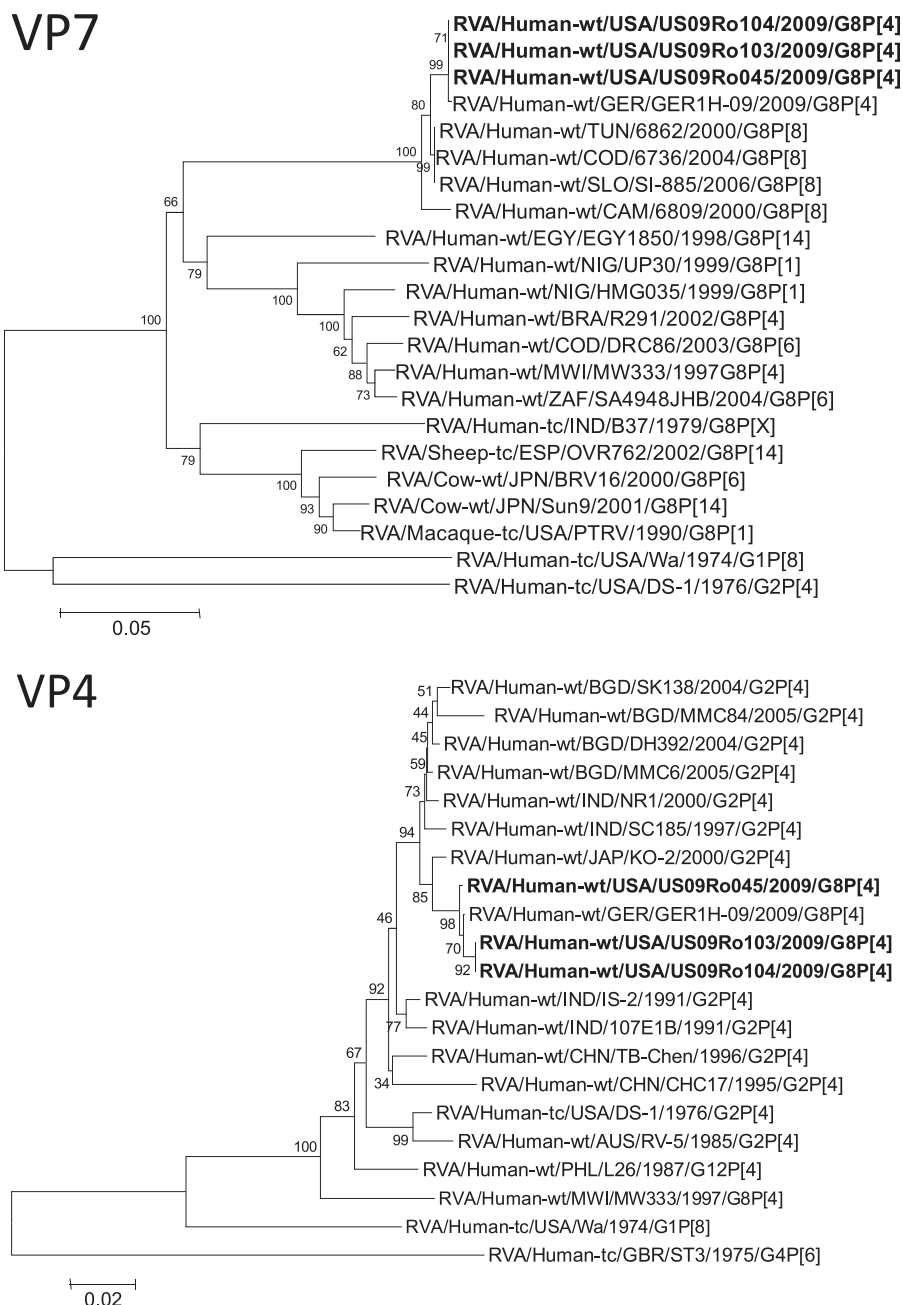


FIG 1 Phylograms indicating genetic relationships of partial VP7 and VP4 nucleotide sequences of the rotavirus strains described in this report (RVA/Human-wt/USA/US09Ro103/2009/G8P[4], RVA/Human-wt/USA/US09Ro104/2009/G8P[4], and RVA/Human-wt/USA/US09Ro045/2009/G8P[4]) (in bold) with representatives of known rotavirus G8 and P[4] genotypes. Evolutionary relationships were inferred by using the neighbor-joining method (30) in the MEGA4 program (33). The *p*-distance model was used to compute the evolutionary distances. The horizontal branch lengths are proportional to the numbers of nucleotide substitutions per site, with the lengths defined by each scale bar. Numbers next to the nodes are percentages of bootstrap support based on 1,000 replicates. The rotavirus group, species of origin, country of identification, common name, year of identification, and G and P genotypes have been indicated for each of the strains.

admitted to the Golisano Children's Hospital at University of Rochester Medical Center with a 2-day history of diarrhea and vomiting (15 to 30 episodes per day). His maximum daily temperature was 37.7°C. He had a complex past medical history of global developmental delay, poor growth, intermittent hematochezia, and coagulopathy of uncertain origin. He lived in the Rochester, NY, metropolitan area and did not have any unusual dietary or

travel exposures in the preceding 3 months; the child did have contact with horses in a therapeutic riding program during this time. The child had not been vaccinated against rotavirus. Moderate dehydration and his baseline levels of hypotonia and choreiform movements were noted upon physical examination; there were no other abnormalities. Intravenous rehydration was administered, and the child improved over the next 1 to 2 days,

although his hospitalization was prolonged for 14 days because of evaluation and institution of therapy for newly diagnosed ulcerative colitis and von Willebrand disease. The child was enrolled in the NVSN at admission. Stool testing was positive for rotavirus antigen by enzyme immunoassay, and subsequent partial VP7 and VP4 gene analysis at the CDC revealed that the isolate was genotype G8P[4].

Licensed U.S. rotavirus vaccines include a pentavalent bovine-human reassortant vaccine containing G1 to G4 and P[8] types (RotaTeq; Merck & Co., Inc.) and a monovalent attenuated human G1P[8] vaccine (Rotarix; GlaxoSmithKline, Inc.) (6). Eighty-five percent of U.S. circulating rotavirus strains have a G or P antigen that is contained in both U.S.-licensed rotavirus vaccines (6, 12). However, >40 human G and P antigen combinations have been reported among the >160 known rotavirus strains (13, 20), and uncommon strains (e.g., G9P[8], G12P[8], and G8P[4]) may suddenly appear in a new geographic area (12, 14, 15, 19, 25, 26). The G9P[8] genotype in particular has emerged to become a globally prevalent strain in a relatively short time since its first description (13, 15, 17, 21).

In ongoing postlicensure surveillance through the CDC NVSN, three children with G8P[4] rotavirus gastroenteritis were detected in Rochester, NY, during the 2009 winter season (December 2008 through June 2009). The 3 G8P[4] rotavirus strains were detected in a total of 183 enrolled children with acute gastroenteritis, 54 (30%) of whom had rotavirus infection. Fifty (94%) of the remaining 51 rotavirus strains were typically found U.S. strains with G or P antigens that are contained in the licensed rotavirus vaccines.

Although not statistically significant, these 3 children were 13 months older on average than the 50 infected with more-typical rotavirus strains (37.3 ± 14.7 months versus 24.2 ± 12.3 months, respectively; $P = 0.26$). No other demographic or clinical differences among these children were found, although all were ill enough to be hospitalized (Table 1). None of the children had unusual travel, dietary, or animal contact; some G8 rotavirus strains infecting humans are thought to reflect a bovine origin (7, 11, 13, 22, 27). This suggests endemic circulation and transmission of the G8P[4] strains in the community, a hypothesis supported by the possible intrafamilial spread in two of the case patients. All 3 children had severe gastroenteritis at onset, although 2 of 3 rapidly recovered with intravenous rehydration and supportive care. None had received any doses of rotavirus vaccines (each was born between 2004 and 2007).

This is the first sequence-confirmed U.S. detection of G8P[4], a strain previously found mainly in Africa (especially Malawi) and sporadically in Europe, Brazil, and Indonesia (7, 8, 11, 34). Sequencing and phylogenetic analysis of partial VP7 and VP4 gene sequences from these 3 G8P[4] strains, designated US09Ro045, US09Ro103, and US09Ro104, revealed that all 3 exhibited 99 to 100% identity with the VP7 and VP4 genes of the 2009 German rotavirus strain GER1H-09 (Fig. 1) and shared phylogenetic lineage with it (27). Full-genome sequencing of these 3 strains is under way (our unpublished data). Although some G8 rotavirus strains have previously been mistyped as G12 strains by genotyping (1), this was not the case for the 3 strains reported herein which were identified and confirmed as genotype G8 by sequencing.

The emergence of G8P[4] strains, which are now being detected in the United States, in several locations in Europe (1, 15, 27) raises questions about the effectiveness of current rotavirus vaccines, which share neither G nor P types with G8P[4] viruses. Similar questions have been raised in the context of a greater prevalence of G2P[4] strains observed after routine implementation of the monovalent G1P[8] rotavirus vaccine in Brazil and in parts of Australia and Belgium (4, 17, 35). However, immunity to rotavirus is believed to be polygenic and likely involves antigens in addition to G and P antigens (9). It is somewhat reassuring that the monovalent G1P[8] vaccine appears to provide good cross-protection against heterologous G8P[4] (18) and G2P[4] (5, 10, 16) rotavirus strains. Nevertheless, mathematical modeling suggests that relatively small differences in effectiveness against particular rotavirus strains could notably alter rotavirus disease dynamics over extended periods of time (2, 28, 29, 31). Thus, continued monitoring is critical to assess whether G8P[4] rotavirus or strains with other unusual genotypes become more prevalent in the United States and globally following the implementation of rotavirus vaccines.

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