JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 1983, p. 663–667
0095-1137/83/090663-05$02.00/0

Vol. 18, No. 3

Rotavirus as a Cause of Severe Gastroenteritis in Adults

PETER ECHEVERRIA,[1]* NEIL R. BLACKLOW,[2] GEORGE G. CUKOR,[2] SANTISOOK VIBULBANDHITKIT,[3] SUCHITRA CHANGCHAWALIT,[1] AND PRAKOUB BOONTHAI[3]

U.S. Component, Armed Forces Research Institute of Medical Sciences, APO San Francisco, California 96346[1]; University of Massachusetts Medical Center, Worcester, Massachusetts 01605[2]; and Bamrasnaradura Hospital, Nonthaburi, Thailand[3]

Received 11 March 1983/Accepted 26 May 1983

Rotavirus was identified as the only etiological agent in 5% of adults (28 of 526) with diarrhea who were admitted to Bamrasnaradura Hospital in Nonthaburi, Thailand, during a 1-year period. Infection was determined by detection of rotavirus in diarrheal stools by enzyme-linked immunosorbent assay accompanied by a greater than fourfold rise in serum complement fixation and radioimmunoassay antibody titers to rotavirus. Adults with clinical rotavirus infections were as severely ill as patients with most bacterial enteric infections; only patients with cholera passed more watery stools and were more dehydrated than those with rotavirus infections. Only 2 of the 28 adults with rotavirus infections had known recent contact with young children with diarrhea. Rotavirus infections in these adults occurred most frequently in the cooler, drier months in Thailand than during the rest of the year. In some settings, rotavirus should be considered in the differential diagnosis of severe diarrhea in adults as well as in young children.

Rotavirus is the most common cause of diarrhea among infants and young children in both developed (3, 12, 15) and developing (1, 17) countries. Diarrhea caused by this virus has also been reported in adults with close contact with infected infants (12, 14) and also in individuals with no obvious contact with young infants (21). Infections in adults have usually been described as mild or subclinical (14, 22). In a hospital in Thailand, we were able to identify a group of adults with rotavirus infection in whom known bacterial pathogens were excluded. We compared the severity of their clinical findings with those of two other groups of diarrhea patients, one group with bacterial enteric infections and the other with no identifiable enteric pathogen.

MATERIALS AND METHODS

The study involved 526 patients over 15 years of age admitted to Bamrasnaradura Hospital, Nonthaburi, Thailand, who had passed at least three stools (which assumed the shape of the container) per 24 h for less than 72 h and had abdominal cramps, vomiting, fever, or prostration. Between 1 October 1980 and 30 September 1981, specimens were collected from each patient on admission, and stool and serum samples were collected again after 3 weeks. Plasma specific gravities were determined to assess the degree of dehydration (16). Stool samples were cultured on selective media and examined for the following accepted or putative enteric pathogens (6): *Salmonella* spp., *Shigella* spp., *Campylobacter* jejuni, *Yersinia enterocolitica*, enterotoxigenic *Escherichia coli*, *Aeromonas hydrophila*, *Plesiomonas shigelloides*, and the vibrios (including O1 and non-O1) *Vibrio cholerae*, *Vibrio parahaemolyticus*, and *Vibrio fluvalis*.

Stool specimens were examined for rotavirus by enzyme-linked immunosorbent assay with guinea pig and goat antisera to the simian rotavirus SA-11 virus (2, 24). Positive specimens were confirmed by radioimmunoassay (RIA) with both pre- and post-immunization antiserum samples (2, 4). Serum antibodies to rotavirus were determined by complement fixation (CF) with SA-11 virus as a substitute antigen for human rotavirus (8) and also by RIA (2, 4).

RESULTS

A total of 28 patients who were not infected with other recognizable enteric pathogens, who were found by enzyme-linked immunosorbent assay to be infected with rotavirus, and who also had greater than fourfold rises in antibody titers to SA-11 virus as determined by CF and RIA, were the subject of this report. As shown in Table 1, 57% (16 of 28) of these adults had, on admission, a CF antibody titer to SA-11 virus of less than 1:2, and 15% (4 of 26) had a titer of less than 1:200 by the more sensitive RIA procedure. Some 64% (18 of 28) were women between 16 and 72 years of age; the 10 infected men were between 25 and 52. Two of 18 women (11%) reported that a family member had also suffered from gastroenteritis within a week of the woman's admission, and both of the family members with diarrhea were children under 5. No family members of males with rotavirus diarrhea had previously been ill.

TABLE 1. Rotavirus infections in 28 adults at Bamrasnaradura Hospital[a]

Patient			Reciprocal of antibody titer			
No.	Age	Sex	Acute phase		Convalescent phase	
			CF	RIA	CF	RIA
1	52	M	<2	200	16	>51,200
2	44	M	2	200	32	51,200
3	16	F	<2	<200	128	800
4	26	F	<2	<200	256	>51,200
5	33	F	<2	800	256	51,200
6	24	F	2	800	128	12,800
7	35	M	<2	<200	128	3,200
8	43	M	16	800	256	>51,200
9	46	F	2	3,200	256	>51,200
10	48	F	2	800	512	3,200
11	36	F	4	3,200	256	12,800
12	32	F	<2	<200	128	12,800
13	25	M	8	3,200	256	12,800
14	27	M	<2	200	256	12,800
15	41	M	<2	200	128	3,200
16	23	M	<2	200	256	12,800
17	72	F	<2	3,200	128	>51,200
18	49	F	4	3,200	256	51,200
19	45	F	8	NT[b]	256	NT
20	23	F	16	NT	256	NT
21	58	F	<2	800	128	>51,200
22	26	F	<2	3,200	256	12,800
23	55	F	<2	800	256	>51,200
24	32	F	<2	200	64	3,200
25	38	F	8	800	512	12,800
26	39	M	8	3,200	64	51,200
27	54	F	<2	200	256	>51,200
28	32	M	<2	800	128	12,800

[a] All patients had rotavirus in their diarrheal stool specimen as determined by enzyme-linked immunosorbent assay.

[b] NT, Not tested.

The clinical characteristics of patients with rotavirus infections and of patients infected with other bacterial enteric pathogens are summarized in Table 2. Patients with rotavirus infections were as ill (as determined by clinical symptoms, extent of stool purging, and plasma specific gravity) as patients with *Shigella* spp., *Salmonella* spp., *V. parahaemolyticus*, enterotoxigenic *E. coli*, and patients in whom no etiological agent was found. No attempts were made to identify other causes of viral enteritis, such as Norwalk virus, coronavirus, and adenovirus. Only individuals with cholera passed more watery stools in a 24-h period and were more dehydrated (as determined by plasma specific gravity) than adults with rotavirus infections. All 28 patients with rotavirus infections left the hospital within 48 h after admission, and only 2 continued to pass watery stools for 24 h after discharge.

As shown in Fig. 1, rotavirus infections were found in 5% of adults (28 of 526) with diarrhea from whom diarrheal stool and acute-phase and convalescent-phase serum samples were examined. Although fewer patients with diarrhea were admitted to the hospital in the winter months, a higher proportion of those patients were suffering from rotavirus infections. Rotavirus infections were more common in the cooler, drier months of January, February, November, and December than the remaining months of the year (17 of 124 versus 11 of 402; $P < 0.001$).

DISCUSSION

Diarrhea caused by rotavirus in adults can be severe, as exemplified by the 28 patients described in this report. In developed countries, 39 to 63% of children hospitalized for acute diarrheal disease are infected with rotavirus (3, 12, 15), and the prevalence of these infections increases in the cooler months of the year (3, 12). In developing countries, a similar proportion of children with diarrhea seen at treatment centers are infected with this virus (1, 19). There are reports of sporadic outbreaks of rotavirus diarrhea in adults. Ryder et al. (18) found that rotavirus was the most frequent etiological agent among Panamanians with diarrhea visiting Mexico, and 4 of 50 U.S. soldiers with diarrhea had serological evidence of recent rotavirus infections during their first 6 weeks in Korea (9). Wenman et al. (22) described 43 rotavirus infection in adults in Canada and found that most infections were mild and occurred most commonly in adults whose children had rotavirus infections. More recently, rotavirus was found in 9% of 2,347 individuals over 10 years of age at a treatment center in Bangladesh (1).

It is clear that host factors are important in susceptibility to infections with gastrointestinal pathogens (5). All of the patients with rotavirus infections were in good health before admission. Yolken described 13 of 22 immunocompromised patients with rotavirus infections who died within 11 days of their infection (23). Although an immunological evaluation was not performed, none of the patients with rotavirus infections described in this report had preceding illnesses which would have compromised their immunological defenses, and all were well within several days of developing gastrointestinal symptoms.

Although intestinal immunoglobulin A antibody to type-specific rotavirus is likely to be important in protection from rotavirus infections, the presence of serum antibody also correlated with resistance to disease in adult volunteers fed rotavirus (13). As in developed countries, serum CF antibody to either SA-11 virus or Nebraska calf diarrhea virus, two substitute antigens for human rotavirus, is acquired by the majority of Thais by 6 years of age (7, 17).

TABLE 2. Comparison of clinical findings associated with different bacterial pathogens and rotavirus in adults at Bamrasnaradura Hospital

Symptom	% of patients for each pathogen showing symptoms						
	Shigella spp. (82)[a]	*Salmonella* spp. (12)	*V. parahaemolyticus* (17)	*V. cholerae* (26)	Enterotoxigenic *E. coli* (24)	No enteric pathogen identified (87)	Rotavirus (28)
Headache	72	100	47	61	46	53	79
Anorexia	73	83	47	54	62	65	68
Malaise	82	92	65	69	71	72	71
Nausea	57	75	59	88	71	70	86
Vomiting	45	66	65	85	46	50	61
Chills	80	92	94	27	67	59	68
Tenesmus	95	100	100	65	83	91	96
Fever	83	75	59	23	62	53	61
Sore throat	36	17	12	4	8	10	11
Cough	12	8	12	19	17	14	11
Coryza	10	8	12	4	4	0	0
Stools per 24 h							
<5	5	8	23	0	12	15	7
5 to 15	78	75	76	42	83	78	68
>15	17	17	0	58	4	7	25
Predominant character of stool							
Watery	6	33	18	88	50	43	61
Mucous	22	50	35	8	33	36	32
Bloody	72	17	47	4	17	21	7
Dehydration[b]	1.0264	1.0283	1.0266	1.0357	1.0275	1.0263	1.0281

[a] Number of patients is shown in parentheses.
[b] Values show mean plasma specific gravity.

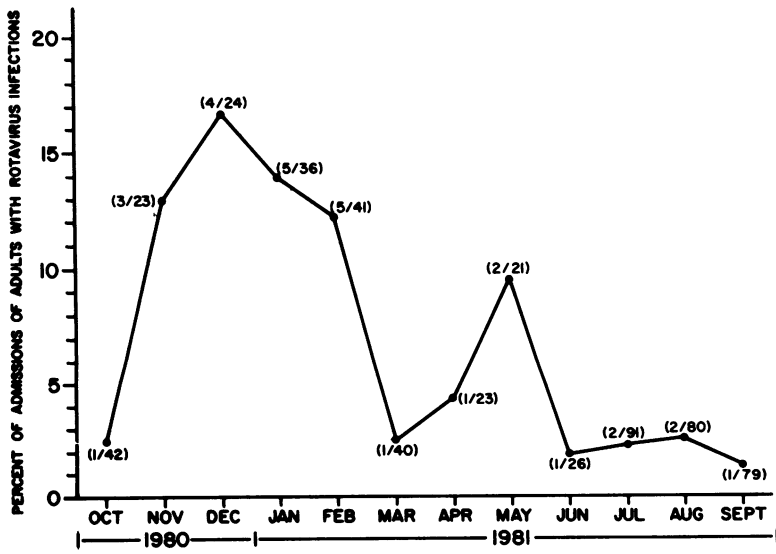

FIG. 1. Percentage of adults with diarrhea due to rotavirus admitted to Bamrasnaradura Hospital between October 1980 and September 1981. Rotavirus infections were determined by the presence of rotavirus in diarrheal stool as detected by enzyme-linked immunosorbent assay accompanied by rises of fourfold or greater in serum CF and RIA antibody titers.

It is not known why some adults are susceptible to rotavirus. Rotavirus type-specific intestinal or serum antibody, infecting dose, concomitant disease, and undefined host or viral genetic differences involved in primary infection and reinfection may be important. Of the adults with rotavirus infections studied in this report, 15% had acute serum antibody titers of less than 1:200 as determined by RIA, which may partially explain their susceptibility to rotavirus infections. However, 25% had acute-phase titers that were 1:3,200, and these patients still became ill. These individuals may have become infected with serotypes of rotavirus with which they had had no previous exposure.

Two of 18 women with rotavirus infections (11%) had young children who also suffered from gastroenteritis; however, none of the 10 men or 16 other women with rotavirus infections had known contact with children with gastroenteritis. Rotavirus can be acquired from young children (12, 14) but may also be acquired in other settings. Travelers with diarrhea (6, 9, 18, 20) and outbreaks of gastroenteritis in adults (10, 11) caused by rotavirus have also been described, implying alternative sources of infection.

Further studies to determine the incidence of type-specific rotavirus infections in adults, especially under conditions in which diarrheal disease is endemic, will be required to determine the importance of this viral enteritis in adults. Rotavirus infections in adults can cause diarrhea as severe as most bacterial enteric infections and should be considered in the differential diagnosis of gastroenteritis in adults as well as in young children.

ACKNOWLEDGMENTS

We thank Sukree Tumrongrachaniti, Sajee Pinnoi, Choompan Manomuth, Pornthip Siripraivan, and Nancy Norwak for assistance in collecting samples and in laboratory investigations.

This research was supported in part by contract DAMD 17-83-C3087 from the U.S. Army Medical Research and Development Command.

LITERATURE CITED

1. **Black, R. E., M. H. Merson, A. S. M. M. Rahman, M. Yunus, A. R. M. A. Alim, I. Huq, R. H. Yolken, and G. T. Curlin.** 1980. A two-year study of bacterial, viral and parasitic agents associated with diarrhea in rural Bangladesh. J. Infect. Dis. **142**:660–664.
2. **Blacklow, N. R., and G. Cukor.** 1980. Viral gastroenteritis agents, p. 891–898. *In* E. H. Lennett, A. Balows, W. J. Hausler, Jr., and J. P. Truant (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.
3. **Brandt, C. D., H. W. Kim, R. H. Yolken, A. Z. Kapikian, J. O. Arrobiol, W. J. Rodriguez, R. G. Wyatt, R. M. Chanock, and R. H. Parrott.** 1979. Comparative epidemiology of two rotavirus serotypes and other viral agents associated with pediatric gastroenteritis. Am. J. Epidemiol. **110**:243–254.
4. **Cukor, G., M. K. Berry, and N. R. Blacklow.** 1978. Simplified radioimmunoassay for detection of human rotavirus in stools. J. Infect. Dis. **138**:906–910.
5. **DuPont, H. L.** 1980. Interactions of enteric pathogens with the intestine, p. 61–65. *In* M. Field, J. S. Fordtran, and S. G. Schultz, Sacretory diarrhea. American Physiological Society, Bethesda, Md.
6. **Echeverria, P., N. R. Blacklow, L. B. Sanford, and G. G. Cukor.** 1981. A study of travelers' diarrhea among American Peace Corps volunteers in rural Thailand. J. Infect. Dis. **143**:767–771.
7. **Echeverria, P., D. S. Burke, N. R. Blacklow, G. Cukor, C. Charoenkul, and S. Yanggratoke.** 1983. Age-specific prevalence of antibody to rotavirus, *Escherichia coli* heat-labile enterotoxin, Norwalk virus, and hepatitis A virus in a rural community in Thailand. J. Clin. Microbiol. **17**:923–925.
8. **Echeverria, P., F. A. Hodge, N. R. Blacklow, J. L. Vollet, G. G. Cukor, H. L. DuPont, and J. H. Cross.** 1978. Travelers' diarrhea among United States Marines in South Korea. Am. J. Epidemiol. **108**:68–73.
9. **Echeverria, P., G. Ramirez, N. R. Blacklow, T. Ksiazek, G. G. Cukor, and J. H. Cross.** 1979. Travelers' diarrhea among U.S. Army troops in South Korea. J. Infect. Dis. **139**:215–219.
10. **Halvorsrud, J., and I. Orstavik.** 1980. An epidemic of rotavirus-associated gastroenteritis in a nursing home for the elderly. Scand. J. Infect. Dis. **12**:161–164.
11. **Holzel, H., D. W. Cubitt, D. A. McSwiggan, P. J. Sanderson, and J. Church.** 1980. An outbreak of rotavirus infection among adults in a cardiology ward. J. Infect. **2**:33–37.
12. **Kapikian, A. Z., H. W. Kim, R. G. Wyatt, W. L. Cline, J. O. Arrobiol, C. D. Brandt, W. J. Rodriguez, D. A. Sack, R. M. Chanock, and R. H. Parrott.** 1976. Human reovirus-like agent as the major pathogen associated with "winter" gastroenteritis in hospitalized infants and young children. N. Engl. J. Med. **294**:965–972.
13. **Kapikian, A. Z., R. G. Wyatt, H. B. Greenberg, A. R. Kalica, H. W. Kim, C. D. Brandt, W. J. Rodriguez, R. H. Parrott, and R. M. Chanock.** 1980. Approaches to immunization of infants and young children against gastroenteritis due to rotavirus. Rev. Infect. Dis. **2**:459–469.
14. **Kim, H. W., C. D. Brandt, A. Z. Kapikian, R. G. Wyatt, J. O. Arrobio, W. J. Rodriguez, R. M. Chanock, and R. H. Parrott.** 1977. Human reovirus-like agent (HRVLA) infection: occurrence in adult contacts of pediatric patients with gastroenteritis. J. Am. Med. Assoc. **238**:404–407.
15. **Konno, T., H. Suzuki, A. Imai, T. Kutsuzawa, N. Ishida, N. Katsuchima, M. Sakamoto, S. Kitaoka, R. Tsuboi, and M. Adachi.** 1978. A long-term survey of rotavirus infection in Japanese children with acute gastorenteritis. J. Infect. Dis. **138**:569–576.
16. **Love, A. H. G., and R. A. Philips.** 1969. Measurement of dehydration in cholera. J. Infect. Dis. **119**:39–42.
17. **Puthavathana, P., N. Vanprapar, K. Thakerngpol, C. Wasi, and P. Thongcharoen.** 1981. Rotavirus infection in Thai people: a preliminary study. J. Med. Assoc. Thailand **64**:341–344.
18. **Ryder, R. W., C. A. Oquist, H. Greenberg, D. N. Taylor, F. Orskov, I. Orskov, A. Z. Kapikian, and R. B. Sack.** 1981. Travelers' diarrhea in Panamanian tourists in Mexico. J. Infect. Dis. **144**:442–448.
19. **Ryder, R. W., D. A. Sack, A. Z. Kapikian, J. C. McLaughlin, J. Chakraborty, A. S. M. M. Rahman, M. H. Merson, and J. G. Wells.** 1976. Enterotoxigenic *Escherichia coli* and reovirus-like agent in rural Bangladesh. Lancet **i**:659–663.
20. **Vollet, J. J., C. D. Ericsson, G. Gibson, L. K. Pickering, H. L. DuPont, S. Kohl, and R. H. Conklin.** 1979. Human rotavirus in an adult population with travelers' diarrhea and its relationship to the location of food consumption. J. Med. Virol. **4**:81–87.
21. **Von Bonsdorff, C. H., T. Hovi, P. Makela, and P. Mort-**

tinen. 1978. Rotavirus infections in adults in association with acute gastroenteritis. J. Med. Virol. **2**:21–28.

22. **Wenman, W. M., D. Hinde, S. Feltham, and M. Gurwith.** 1979. Rotavirus infections in adults: results of a prospective study. N. Engl. J. Med. **301**:303–306.
23. **Yolken, R. H., C. A. Bishop, T. R. Townsend, E. A. Bolyard, J. Bartlett, G. N. Santos, and R. Saral.** 1982. Infectious gastroenteritis in bone-marrow transplant recipients. N. Engl. J. Med. **306**:1009–1012.
24. **Yolken, R. H., H. W. Kim, T. Clem, R. G. Wyatt, A. R. Kalica, R. M. Chanock, and A. Z. Kapikian.** 1977. Enzyme-linked immunoassay (ELISA) for detection of human reovirus-like agent of infantile gastroenteritis. Lancet **ii**:263–266.