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National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
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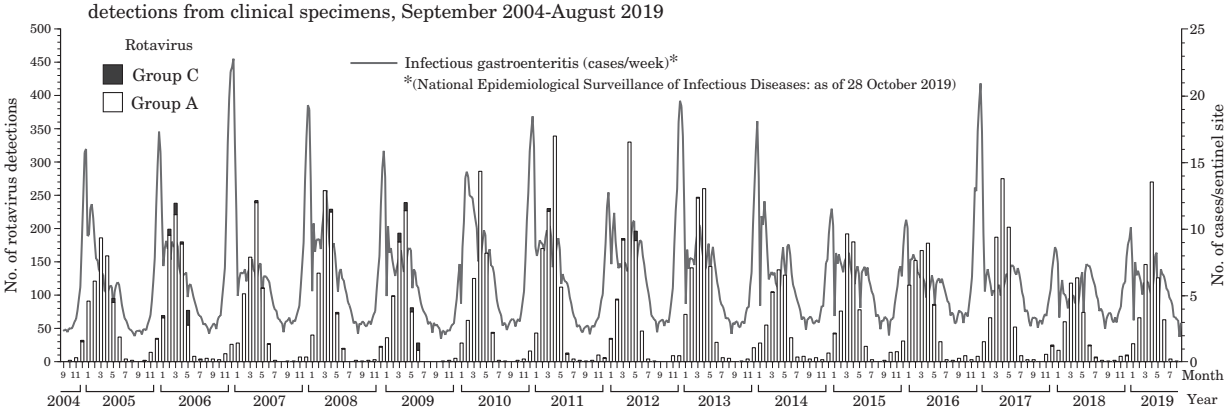
<THE TOPIC OF THIS MONTH>
Rotavirus, from September 2004 to August 2019, Japan

Figure 1. Weekly number of reported infectious gastroenteritis cases from sentinel sites and monthly number of reported rotavirus detections from clinical specimens, September 2004-August 2019



(Infectious Agents Surveillance System: as of 23 October 2019)

Rotavirus is a double-stranded RNA virus of 11 segments categorized into the genus *Rotavirus* belonging to the family *Reoviridae*. Rotavirus has no envelope and is classified into nine species (group A to I). The rotaviruses that have been reported to infect humans are mainly groups A and C, and epidemics among humans are mostly caused by group A. Rotavirus is a major cause of acute viral gastroenteritis in infants, and the majority of people are believed to have experienced infection at least once by 5 years of age. The virus is transmitted via the fecal-oral route, and usually with an incubation period of 2-4 days, causes symptoms such as diarrhea, vomiting, and fever. There is no specific therapy, and symptomatic treatments, such as infusion and oral rehydration, are performed. Although patients usually recover within a week, dehydration is often more severe than in other types of viral gastroenteritis. Convulsion associated with gastroenteritis is one of the complications, which is characterized by a cluster of convulsions 1-6 days (average 2.3 days) after acute gastroenteritis onset (see p. 209 of this issue). Less frequent complications include renal or hepatic failure and encephalitis/encephalopathy. Many of the severe cases are reported in children at primary infection during the period from 6 months to 2 years old. Treatment is performed according to the level of complication.

Infectious gastroenteritis under the National Epidemiological Surveillance of Infectious Diseases (NESID) system: Under the Infectious Diseases Control Law, rotavirus infection is included under "infectious gastroenteritis" (notification criteria: https://www.niid.go.jp/niid/images/iasr/35/409/de4091.pdf), a Category V infectious disease to be reported from approximately 3,000 nationwide pediatric sentinel clinics. Every year, the number of reports of patients with "infectious gastroenteritis" sharply increases from November to December, peaks gently from February to May, and then declines (Fig. 1). The February-May peak of infectious gastroenteritis overlaps with the rotavirus detection peak, and the November/December peak overlaps with the norovirus detection peak (https://nesid4g.mhlw.go.jp/Byogentai/Pdf/data11j.pdf).

According to an amendment of the Regulation for Enforcement of the Infectious Diseases Control Law, the designated sentinel sites (approximately 500 medical institutions nationwide) have been requested to report patients with "gastroenteritis specifically caused by rotavirus infection" since October 14, 2013 (notification criteria: https://www.niid.go.jp/niid/images/iasr/35/409/de4092.pdf).

Reports of rotavirus detection from public health institutes: Prefectural and municipal public health institutes (PHIs) carry out laboratory diagnosis of infectious gastroenteritis cases based on fecal specimens sent from approximately 10% of the pediatric sentinel clinics and also from specimens collected from outbreaks (the Infectious Agents Surveillance System). During the 2004/05-2009/10 seasons, 700-800 rotavirus detections/year were reported, but this number increased to approximately 900/year during the

(Continued on page 202′)

(THE TOPIC OF THIS MONTH-Continued)

2010/11-2012/13 season. During the 2013/14-2018/19 seasons, the number periodically changed between 500-800/year (Table 1 and Fig. 2 in p. 203). Group A rotavirus accounted for the majority, with few group C detections (the highest was 6% in the 2005/06 and 2008/09 seasons, and it has been less than 0.2% since the 2012/13 season). Group B rotavirus has not been reported in Japan.

The age distribution in 10,770 cases of group A rotavirus detected between September 2004 and August 2019 was in the order of 1-year-olds (34%), 2-year-olds (17%), and 0-year-olds (16%), and children under 2 years of age accounted for approximately two-thirds of the patients whose age was known (Fig. 3 in p. 203). Among those aged <1 year, those aged 6 months or older composed the majority. The same age distribution was observed across genotypes G1, G3, and G9. Although the detection number of genotypes G8 was slightly lower, this genotype had a slightly different age distribution; the proportion of 5-9 years was the highest, followed by those aged 1-year-olds and 2 years. On the other hand, of the 150 group C rotavirus-detected cases, children aged 5-9 years were the most common, accounting for approximately one half, followed by children aged 10-14 years accounting for approximately 19%.

Genotyping of group A rotavirus: The genome of group A rotavirus consists of 11 gene segments of double-stranded RNA. As the genotypes of the two proteins possessing neutralizing antigenic sites, VP7 (outer capsid protein, G type) and VP4 (spike protein, P type), reflect serotypes, the investigation of these two genotypes has been emphasized. In Japan, some PHIs conduct G-genotyping and report the results (Table 1 and Fig. 2 in p. 203). In addition, some research groups also conduct surveillance of epidemic strains inside and outside of the country (see p. 204 of this issue). Before vaccine introduction, the major epidemic group A rotavirus detected in humans was considered to comprise 5 genotypes, G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8]. In recent years, however, previously rare genotypes (G8), strains with genes thought to have originated from animal rotaviruses (bovine-like G8 and equine-like G3), and strains with new genotype constitutions (DS-1-like G1P[8], DS-1-like G3P[8], and G9P[8]-E2) have been reported in Japan and overseas (see pp. 207 and 208 of this issue). The Department of Virology II, National Institute of Infectious Diseases, has designed a new primer set to accurately detect the G-genotypes that have become prevalent in recent years (see p. 205 of this issue).

Complications: Since October 14, 2013, the number of cases of "gastroenteritis specifically caused by rotavirus infection" reported from the designated sentinel sites was 26,716 (as of December 4, 2019) The majority (98%) were in children under the age of 15, accounting for 26,073 cases, whereas 602 (2%) were in adults over the age of 20 years. Of the 6,018 cases of acute encephalitis reported between Week 1 of 2007 and Week 43 of 2019, rotavirus (including other pathogens) was described as the causative or detected pathogen (rotavirus encephalopathy) in 160 cases (as of November 6, 2019). Rotavirus encephalopathy was reported frequently from March to May, and coincided with the period when "gastroenteritis specifically caused by rotavirus infection" was reported (see p. 210 of this issue).

Outbreak: Rotavirus outbreaks occur frequently in nurseries and kindergartens, but are also common in primary schools, junior high schools, nursing homes for the elderly, and welfare facilities (Table 2 in p. 203). Among the rotavirus gastroenteritis outbreaks in 2004-2018, 219 were group A and 35 were group C (Table 2 in p. 203).

Prevention: Rotavirus is stable in the environment and its infectivity is very high. As many as 10^{10} viruses are excreted in one gram of diarrheal stool of infected persons, the prevention of rotavirus infection is markedly difficult even in developed countries where sanitation is improved.

The purpose of the rotavirus vaccine is to acquire immunity with the vaccine before the primary infection, which is most likely to become severe, and to prevent severe gastroenteritis. Currently, there are two oral attenuated live vaccines, G1P[8] monovalent vaccine and a pentavalent vaccine containing G1-G4 and P[8] antigens, which are in routine vaccination in more than 80 countries. World Health Organization (WHO) has stated that current rotavirus vaccines are safe except for a slight increase in the risk of intussusception within 7 days of primary administration (up to 1-2 increase/100,000), and the benefits of preventing severe gastroenteritis and related death far outweigh the increased risk of intussusception (https://www.who.int/vaccine_safety/committee/topics/rotavirus/rotarix_and_rotateq/dec_2017/en/). The vaccines have been available for voluntary inoculation since November 2011 and July 2012, respectively, in Japan. Epidemiological analysis has demonstrated high vaccine effectiveness against hospitalized cases of rotavirus infection in children under 5 years and reductions in hospitalization rates in several parts of Japan (see p. 212 of this issue).

Challenges: In Japan, the Committee on Immunization and Vaccine, Health Science Council of Ministry of Health, Labour and Welfare decided to introduce the rotavirus vaccine as a routine vaccination from October 1, 2020. The main challenge in the future is to monitor the effectiveness and safety of the vaccines introduced in Japan. Therefore, 1) it is necessary to accurately understand the trends in the incidence of rotavirus infections, especially in severe cases, before and after the introduction of the vaccine. 2) Regarding safety, the importance of carefully monitoring the incidence of intussusception after vaccine introduction has been emphasized (see p. 213 of this issue). 3) Moreover, the system to monitor virological changes in wild strains caused by the selective pressure of vaccines must be improved and strengthened.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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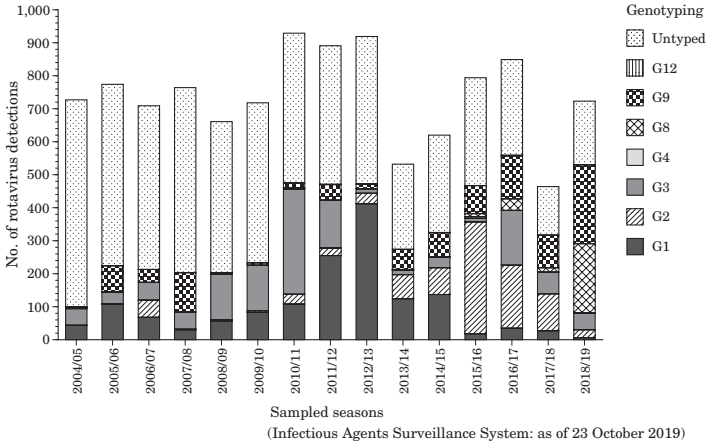
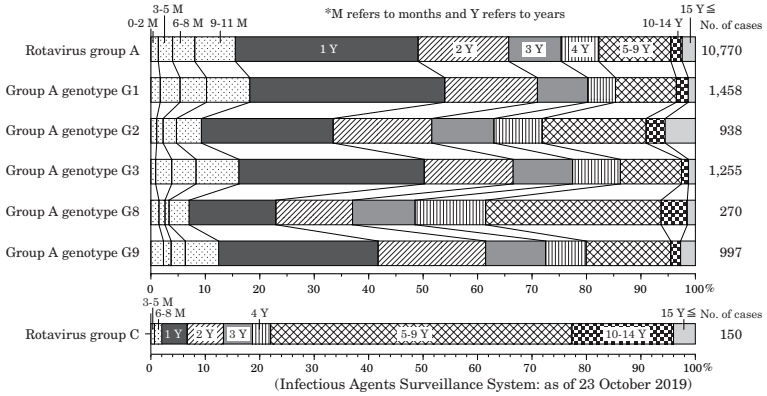
(THE TOPIC OF THIS MONTH-Continued)

Figure 2. Genotyping of group A rotaviruses 2004/05-2018/19



(Infectious Agents Surveillance System: as of 23 October 2019)

Figure 3. Age distribution of patients from whom rotavirus was detected, September 2004- August 2019



(Infectious Agents Surveillance System: as of 23 October 2019)

Table 1. Detection of rotaviruses during 2004/05-2018/19 seasons

Group/ genotype	Detection from specimens collected during September through August in the following year														
	2004/05	2005/06	2006/07	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19
Group unknown	3	4	1	1	–	6	4	–	1	–	3	–	–	2	1
Group A	727	774	709	764	661	718	929	891	919	532	620	794	849	464	723
Not typed	628	550	496	561	458	485	454	420	447	258	295	327	290	147	193
G1	44	107	68	30	57	83	108	255	412	124	137	18	35	27	6
G2	–	2	52	2	4	5	30	23	32	73	81	339	191	112	24
G3	50	35	54	52	138	138	318	144	13	13	33	11	166	66	51
G4	4	–	–	–	–	–	4	1	–	1	–	5	–	–	–
G8	–	1	–	–	–	–	–	–	–	2	1	9	35	13	210
G9	1	79	39	119	4	7	15	47	15	61	72	85	130	99	239
G12	–	–	–	–	–	–	–	1	–	–	1	–	2	–	–
Group C	8	57	5	7	44	1	6	19	1	1	1	1	–	4	1
Total	738	835	715	772	705	725	939	910	921	533	624	795	849	470	725

(Infectious Agents Sureveillance System: as of 23 October 2019)

Table 2. Number of rotavirus infection outbreaks, 2004-2018

Suspected place of infection	Year of onset															Total
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	
Unknown	–	–	–	–	–	–	–	–	4	2	–	–	–	–	–	6
Hotel・inn (except for banquet hall)	–	–	1(1)	–	–	–	–	–	–	–	–	–	–	–	–	1(1)
Restaurant	–	–	1	–	–	–	–	–	2	–	–	–	–	–	1	4
Nursery	–	2	3(1)	2	6	3	16	12	24	7	9	3	10	10	2	109(1)
Kindergarten	3	2	1	–	1	1	–	1	4	–	1	–	2	–	1	15
Elementary school	1	3(2)	10(10)	–	10(6)	5(5)	1	6	9(1)	3(1)	2	3	4	3	2	62(25)
Junior high school	–	–	–	–	–	1(1)	–	–	2	–	–	–	–	–	–	3(1)
High school	–	–	–	–	–	–	–	–	1	–	–	1	–	–	–	2
Dormitory	–	–	–	–	–	–	–	–	1	–	–	–	–	–	–	1
Hospital	–	–	–	–	–	–	–	–	–	–	1	–	–	–	–	1
Nursing home (include nursing facility)	1	4	2	2	–	1	1	1	1	1	–	–	4	1	2	21
Welfare facility	1(1)	–	5(1)	–	2(2)	–	1	4	–	–	3	–	1	2(1)	2	21(5)
Others	–	–	1	1	–	1(1)	–	1(1)	–	–	–	–	–	2	2	8(2)
Total	6(1)	11(2)	24(13)	5	19(8)	12(7)	19	25(1)	48(1)	13(1)	16	7	21	18(1)	12	254(35)

*Data based on “Report of pathogens that caused the outbreak” from Prefectural and municipal public health institutes.
Number in parentheses refer to number of rotavirus group C outbreaks (reshown).
(Infectious Agents Sureveillance System: as of 23 October 2019).