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National Institute of Infectious Diseases and
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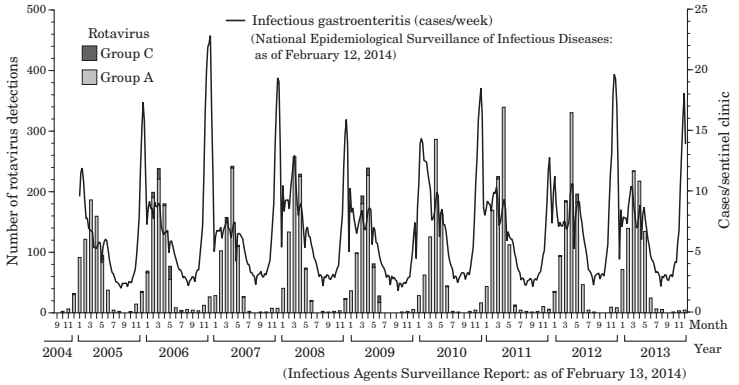
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Rotavirus, 2010-2013, Japan

Rotavirus belongs to the family *Reoviridae*, whose genome consists of 11 segments of double-stranded RNA. Rotavirus is classified into groups A-G according to the inner core protein's antigenicity, among which groups A-C are detected from humans. Group A rotavirus is often referred to simply as "rotavirus" since this group makes up most of the circulating rotavirus in the world. Rotavirus is a major cause of acute viral gastroenteritis among infants, and majority of the people are believed to have experienced infection at least once by 5 years of age (see p. 65 of this issue). The virus is transmitted by the fecal-oral route, and after an incubation of 1-4 days, clinical manifestations consisting of diarrhea, vomiting and fever appear. Treatment is oral or intravenous rehydration, as no specific treatment is available. While patients usually recover within a week, dehydration is often more severe compared with other viral gastroenteritis. Complications include seizures, which, if sustained, are associated with poor prognosis and increased risk of sequelae. Less frequent complications include renal or hepatic failures and encephalitis/encephalopathy. Although rare in developed countries, much of pediatric diarrheal deaths in developing countries is attributed to rotavirus infection (estimated 450,000 deaths/year) (Lancet Infect Dis 12: 136-141, 2012).

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 in http://www.nih.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. An amendment on 14 October 2013 introduced an additional reporting system; approximately 500 select key medical institutions (sentinel hospitals) in Japan are requested to notify patients of "gastroenteritis specifically caused by rotavirus infection" (notification criteria in http://www.nih.go.jp/niid/images/iasr/35/409/de4092.pdf). If a pediatric sentinel clinic is selected as a key medical institution, the clinic is requested to notify a rotavirus gastroenteritis patient as "infectious gastroenteritis" and also as "infectious gastroenteritis specifically caused by rotavirus infection". With these measures, it is believed that epidemiologic features of rotavirus infection (particularly those of severe cases) will become clearer.

Figure 1. Weekly number of infectious gastroenteritis cases reported from sentinel clinics and monthly number of rotavirus detections from clinical specimens, September 2004-December 2013



Every year, "infectious gastroenteritis" increases sharply during November/December with a wide peak in February/March to May followed by a decline (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://nesid3g.mhlw.go.jp/Byogentai/Pdf/data11e.pdf).

Table 1. Detection of rotaviruses during 2005/06-2013/14 seasons

Group/genotype	Detections from specimens collected during September through August in the following year*								
	2005/06	2006/07	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14
Group unknown	4	1	1	-	6	7	-	2	-
Group A	774	709	764	661	718	923	891	846	17
Not typed	550	496	561	458	485	487	447	494	14
G1	107	68	30	57	83	104	243	302	-
G2	2	52	2	4	5	23	22	29	-
G3	35	54	52	138	138	292	132	10	2
G4	-	-	-	-	-	2	-	-	-
G8	1	-	-	-	-	-	-	-	-
G9	79	39	119	4	7	15	46	11	1
G12	-	-	-	-	-	-	1	-	-
Group C	57	5	7	44	1	6	19	1	-
Total	835	715	772	705	725	936	910	849	17

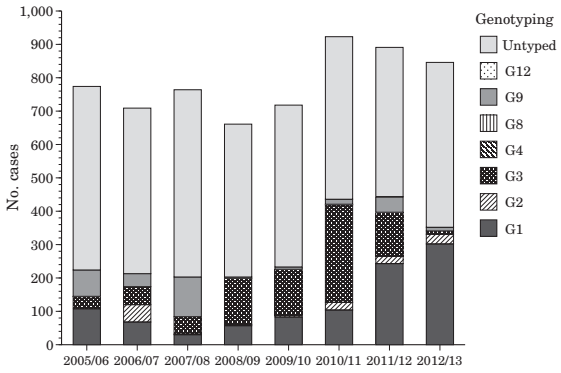
*Data based on reports received from local public health institutes.
(Infectious Agents Surveillance Report: as of February 13, 2014)

Reports of rotavirus detection from public health institutes: Prefectural and municipal public health institutes (PHIs) conduct 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 out-

(Continued on page 64′)

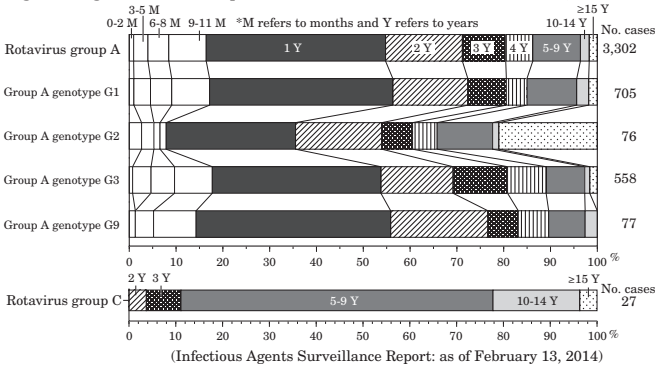
(THE TOPIC OF THIS MONTH-Continued)

Figure 2. Genotyping of group A rotaviruses 2005/06-2012/13 seasons



(Infectious Agents Surveillance Report: as of February 13, 2014)

Figure 3. Age distribution of patients from whom rotavirus was detected, 2010-2013



(Infectious Agents Surveillance Report: as of February 13, 2014)

Table 2. Number of rotavirus infection outbreaks, 2010-2013*

Suspected place of infection	Year of onset				Total
	2010	2011	2012	2013	
Nursery	16	12	24	7	59
Primary school	1	6	9 (1)	3 (1)	19 (2)
Welfare facility	1	4	-	-	5
Kindergarten	-	1	4	-	5
Nursing home	1	1	1	1	4
Restaurant	-	-	2 **	-	2
Junior high school	-	-	2	-	2
High school	-	-	1	-	1
Dormitory	-	-	1	-	1
Other/Unknown	2	2 (1)	4	2	10 (1)
Total	21	26 (1)	48 (1)	13 (1)	108 (3)

*Data based on reports received from local public health institutes.
**2 foodborne outbreaks
Numbers in parentheses refer to number of rotavirus group C outbreaks.
(Infectious Agents Surveillance Report: as of February 13, 2014)

breaks. During the past 4 years from 2010 to 2013, 60 PHIs reported group A and 8 PHIs reported group C rotavirus detections. During 2005/06-2009/10 seasons, 700-800 rotavirus detections/year were reported, but increased during 2010/11 (Table 1, Fig 2). Group A rotavirus has been the majority with few group C detections (0.1-2.2% since 2010/11 season). Group B rotavirus has not been reported in Japan.

Genotyping of group A rotavirus: Group A rotavirus is classified according to combination of serotype-related G and P genotypes, which are respectively determined by the genetic sequences of the outer-layer capsid proteins VP7 and VP4 (neutralizing antibody epitopes). Most human isolates are currently G1P[8], G2P[4], G3P[8], G4P[8], and G9P[8] (see p. 66 of this issue). Currently, some PHIs are conducting G genotyping (see pp. 67-71 of this issue).

Among 3,302 patients from whom group A rotavirus were detected during 2010-2013, 38% were 1 year of age, 16% <1 year of age, and 16% 2 years of age; children under 2 years of age comprised 70% of the patients whose age was known (Fig. 3). Among those <1 year, those aged 6 months or older composed the majority. The same age distribution was observed across genotypes G1, G3 and G9. Genotype G2 had a slightly different age distribution; following those aged 1 year (28%), those aged ≥15 years were frequent (21%). Of the 27 group C rotavirus-detected cases, 18 were children aged 5-9 years and 5 were children aged 10-14 years.

Complications: During 2010-2013, rotavirus was detected in 22 cases of encephalitis/encephalopathy and 4 cases of meningitis had rotavirus detection. Additionally, group A rotavirus was detected from 4 cases of intussusception.

Outbreak incidents: Rotavirus outbreaks occur frequently in nurseries and in kindergartens, but also occasionally in primary schools, junior high schools, nursing homes for the elderly, and welfare facilities (IASR 33: 13-14, 2012; *ibid*. 33: 197-198, 2012; *ibid*. 33: 271, 2012; *ibid*. 34: 69-79, 2013; *ibid*. 34: 264-265, 2013) (Table 2). Among rotavirus gastroenteritis outbreaks in 2010-2013, 105 were group A and 3 group C (Table 2). Majority of these incidents were attributable to person-to-person transmission except for two food poisoning outbreaks caused by group A rotavirus. Five outbreaks involved more than 50 patients (4 outbreaks due to group A and 1 outbreak due to group C); two were in April-May 2011 and three March-April 2012.

Prevention: Rotavirus's infectivity is very high and 10-100 virions are sufficient in establishing infection. An infected patient's stool contains as many as 10^{10}-10^{11} virions per gram, making rotavirus prevention difficult even in developed countries where sanitation and hygiene are well developed. Currently two oral attenuated live vaccines, G1P[8] monovalent vaccine and a pentavalent vaccine containing G1-G4 and P[8] antigens, have been approved and used in more than 130 countries for preventing severe outcomes and introduced as a routine immunization in 53 countries (see p. 71 of this issue). The vaccines are available on a voluntary basis since November 2011 and July 2012, respectively, in Japan. The estimated vaccine coverage among the target age population was 35% in July 2012, and 45% in April 2013 (see p. 73 of this issue).

Challenges: Japan is currently evaluating incorporation of rotavirus vaccine as a routine immunization. Studies from abroad have indicated that rotavirus vaccine can prevent an estimated 90% of severe outcomes due to rotavirus infection in developed countries (The Immunization and Vaccine Committee of the Health Science Council, Basic Direction of Immunization Policy Subcommittee, Rotavirus Vaccine Task Force Interim Report, 18 November 2013). If rotavirus vaccination is to be introduced in Japan, its effectiveness and safety must be evaluated by: 1) monitoring trends in rotavirus cases, particularly of severe ones; 2) with regards to safety, given the slight increase in the incidence of intussusception reported from countries that have implemented rotavirus immunization, there is a need for careful monitoring of the occurrence of intussusception (see p.74 of this issue); and 3) to monitor the virus populations in circulation, considering vaccination's potential selection pressure on circulating rotaviruses. Rotavirus surveillance should thus be further strengthened and coordinated between the National Institute of Infectious Diseases and partners such as PHIs and universities.

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 Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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